UNIVERSIDAD AUTONOMA DE MADRID

UNIVERSIDAD COMPLUTENSE DE MADRID

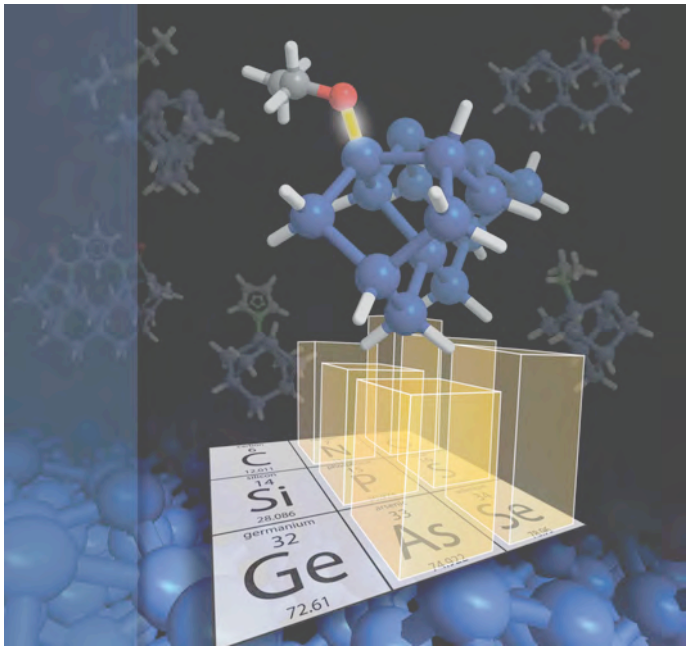
USC UNIVERSIDADE DE SANTIAGO DE COMPOSTELA

MASTERQO

MÁSTER UNIVERSITARIO EN QUÍMICA ORGÁNICA

X Simposio

Máster Interuniversitario en Química Orgánica



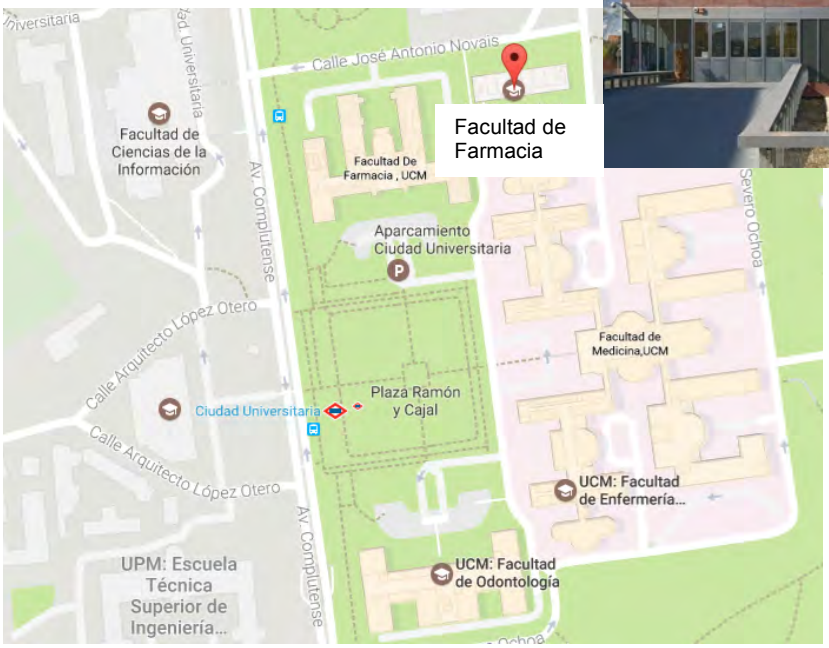
Universidad Complutense de Madrid

22 y 23 de Junio de 2017

INFORMACIÓN GENERAL

X Simposio del Máster Interuniversitario en Química Orgánica

El Simposio tendrá lugar en el Aulario de la Facultad de Farmacia de la Universidad Complutense de Madrid. Las conferencias se impartirán en la Sala Cofares y los pósteres en la planta baja del mismo edificio.



Dirección: Plaza Ramón y Cajal s/n. Ciudad Universitaria. 28040 Madrid
Cómo llegar:
Metro: Línea 6 (circular). Estación: Ciudad Universitaria
Autobuses: líneas 82, 132, F, G y U

PROGRAMA

X Simposio del Máster Interuniversitario en Química Orgánica

Universidad Complutense de Madrid
Aulario de la Facultad de Farmacia (Sala Cofares)

22 de Junio de 2017

12:00 Apertura
12:15 Conferencia: “Drug discovery evolution in the last decade”. Dra. Mª Ángeles Martínez Grau (Eli Lilly)
13:30 Almuerzo
16:00 Conferencia: “Química y política” Dr. Alfredo Pérez Rubalcaba (UCM)
17:00 Pausa Café
17:30 Sesión de Pósteres I

23 de Junio de 2017

9:30 Sesión de Pósteres II
11:30 Pausa Café
11:45 Sesión de Pósteres III
13:30 Almuerzo
16:30 Conferencia: “Resolución de problemas químico-forenses: casos prácticos”. Dr. Alfonso Vega García (UICP y UAH)
17:30 Clausura

ORGANIZACIÓN

Comité Organizador Local

David García Fresnadillo (UCM)
Mar Gómez Gallego (UCM)
Silvia Ortega Gutiérrez (UCM)

Departamento de Química Orgánica I, Facultad de Ciencias Químicas, Universidad Complutense de Madrid

Comité Interuniversitario

José Alemán (UAM)
Belén Cid de la Plata (UAM)
Ramón J. Estévez Cabanas (USC)
Alberto Fraile Carrasco (UAM)
Mercedes Rodríguez Fernández (UAM)
Juan Carlos Rodríguez Ubis (UAM)

UAM UNIVERSIDAD AUTONOMA DE MADRID

USC UNIVERSIDADE DE SANTIAGO DE COMPOSTELA

PARTICIPANTES

Aguado de Blas, Laura M.	UAM	P1
Aguado Rivero, Sergio	UCM	P2
Alberca Manzano, Saúl	UCM	P23
Alonso de la Peña, Miguel	UAM	P26
Álvarez Fernández, Delia	UAM	P28
Aparicio Gil, Borja	UCM	P29
Barbón, N.	USC	P30
Boga, S.	USC	P55
Buendía Mateos, Manuel	UCM	P31
Burgos Redondo, Imanol	UCM	P3
Calvo Martín, Gorka	UCM	P32
Canal Martín, Andrea	UCM	P4
Cantero Rivas, Gabriela	UCM	P56
Carballo Pedrares, N.	USC	P5
Carrión Rus, Álvaro	UCM	P33
Chamorro Zabalza, Paula Blue	UAM	P34
Cendón Mariño, Borja	USC	P6
Corpas Pardo, Javier	UAM	P7
Díaz Casado, Laura	UCM	P57
Escobar Peña, Ana Andrea	UCM	P60
Espiñeira Gutiérrez, Adrián	UCM	P35
Fernández Cabello, Víctor	UAM	P8
Figuerola Femenias, Andreu	UCM	P61
Franco Fernández, Mario	UAM	P9
Gallego Gómez, Iván	USC	P36
Garcés Garcés, José	UCM	P10
García Fernández, Pedro David	UCM	P63
García Vázquez, Víctor	UAM	P38
Garrido González, José Javier,	UCM	P24
González Blázquez, Borja	UAM	P11
González Molina, Álvaro	UCM	P37
Humbrías Martín, Jorge	UAM	P12
Iniesta Bernabé, Manuel	UAM	P58
Izquierdo García, Carolina	UAM	P59
Jiménez Vicent, Diego	UCM	P39
Lago, Xade	USC	P73
López Blanco, R.	USC	P27
López García, Antonio	UCM	P25
López Martínez, Javier	UCM	P13
Maquillón Albaladejo, Cristina	UAM	P71
Mariño Fernández, Fátima	USC	P40
Martínez Gualda, Ana María	UAM	P62
Mayo Mariscal de Gante, Paloma Pilar	UCM	P65
Merí Bofí, Laura	UCM	P41
Molina Ferreiro, Francisco	USC	P14
Nieto Carmona, Juan Carlos	UAM	P15

Novoa Rodríguez, Luis Manuel	UCM	P42
Orozco González, Óscar	UCM	P72
Ortega Fernández-Pacheco Pablo	UCM	P16
Palop Clares, Pedro Guillermo	UCM	P18
Pena, Celia	USC	P43
Ramírez Barroso, Sergio	UCM	P44
Rivadulla Cendal, Elena	USC	P45
Rodríguez Álvarez, Sandra	USC	P17
Rodríguez Costa, Ángela	USC	P69
Rodríguez Díaz, Ciro	UAM	P46
Rodríguez Salamanca, Patricia	UAM	P48
Romero Muñiz, Ignacio	UCM	P19
Rubio González, Saúl	UAM	P66
San Jacinto García, Jorge	UCM	P47
Sánchez Galán, Mercedes	UAM	P50
Sánchez Naya, Roberto	UCM	P49
Sánchez-Cid Muñoz, Cristina	UCM	P52
Simón Marqués, Pablo	UAM	P51
Socias Pinto, L.	USC	P20
Spear, Luke Anthony	UCM	P70
Suarez Barrigón, L.	USC	P53
Toledano Pinedo, Mireia	UCM	P21
Torre Jarrín, Isabel de la	UAM	P67
Torres Ruiz, Alejandro	UCM	P54
Vázquez Galiñanes, N.	USC	P64
Vidal, Xandro	USC	P68
Villacampa San Agustín, Alejandro	UCM	P22
Yonte Pindado, Elena	UAM	P74

ABSTRACTS

Nickel-catalyzed reactions for the formation of alkyl-alkyl and alkyl-nitrogen bonds.

L. Aguado Deblas, G. Caballero Santiago, D.J. Cárdenas, M. Rodríguez-Fernández.

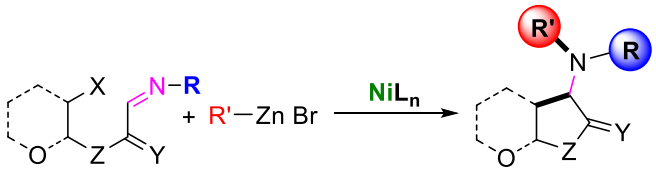
Departamento de Química Orgánica, Facultad de Ciencias, Universidad Autónoma de Madrid
e-mail: lauram.aguado@estudiante.uam.es

***Keywords**: Negishi, Nickel, cyclization-coupling.*

The transition metals-catalyzed coupling reactions have become a fundamental synthetic tool to the formation of carbon-carbon and carbon-heteroatom bonds. Nowadays, these methods have important applications in fields such as the synthesis of natural products, organic materials and pharmaceutical compounds.[1]

In this scope, imines and derivatives are known to be excellent radical acceptors and different radical cyclization promoted most of them by tributyltin hydride are described in the literature.[2] However, the high toxicity of this reagent has made it necessary to search other alternatives. The use of first row transition metals, like Ni, is a suitable choice because this element is inexpensive, environmentally benign, has low toxicity and ready access to multiple oxidation states.

Recently, Cardenas group has achieved the formation of two $C(sp^3)$-$C(sp^3)$ bonds in a single operation by sequential cyclization and nickel-catalysed Negishi-type cross-coupling of alkyl zinc bromides with iodoalkanes containing an alkene group.[3] Based on these background, the purpose of this project is the study of nickel-catalysed cyclization and/or coupling reactions for the formation of $C(sp^3)$-$C(sp^3)$ and $C(sp^3)$-N bonds in a single synthetic operation. Alkyl halides functionalized with C-N double bonds and alkylzinc bromides will be employed.



Z = CH_2, O, NTs, $C(CO_2Et)_2$; Y = H_2, O;

R= OMe, OBn, NPh_2; **R'** = Alq.

[1] Tsuji, J, *Palladium Reagents and Catalysts*; Wiley & Sons, Chichester, **1995**, 345-356; Diederich F., de Meijere A.; *Metal-catalized Cross-Coupling Reactions*, 2nd ed.,Wiley-VCH: Weinheim, **2004**; Magano, J., Dunetz, J. R. *Chem. Rev.* **2011**, *111*, 2177-2250.
[2] Liu D., Liu C., Lei A. *Chem. Asian J.* **2015**, *10*, 2040; Miyabe H., Ueda M., Takeaki N., *Synlett*, **2004**, *7*, 1140-1157.
[3] Phapale, V. B., Bunuel, E., Garcia-Iglesias, M., Cardenas, D. J. *Angew. Chem. Int. Ed.*, **2007**, *46*, 8790-8795.

Synthesis of New Iron Hydrogenases Mimics

Sergio Aguado, Alba D. Merinero, Luis Casarrubios, Miguel A. Sierra.

Departamento de Química Orgánica I, Facultad de Ciencias Químicas, Universidad Complutense de Madrid, 28040 Madrid (Spain). Centro de Innovación en Química Avanzada (ORFEO-CINQA), Facultad de Ciencias Químicas, Universidad Complutense de Madrid.

sergioag@ucm.es

***Keywords**: Hydrogenases, cycloaddition, iron cluster.*

Our main objective is the development of hydrogenasas mimetics modulable by transition metals for the production of hydrogen. The hydrogenasas are metalloenzymes of bacterial metabolism responsible to catalyze the conversion of protons into molecular hydrogen.

Different metallocenes will be combined with the iron cluster $[(\mu\text{-}SCH_2)Fe_2(CO)_6]$ to achieve the analogues of hydrogenase using a copper-catalyzed 1,3-dipolar cycloaddition. The comparative electrochemical study between the cycloaddition products and the starting azide will show the modulation of the properties of the cluster by the introduction of new metal atoms in the structure.

References:

1. Casarrubios, L; de la Torre, M. C.; Sierra, M. A. *Chem. Eur. J.* **2013**, 3534-3541.
2. **(a)** Yulong, L; Rauchfuss, T.B. *Chem. Rev.* **2016**, 7043-7077. (b) Lubitz, W.; Ogata, H.; Rüdiger, O.; Reijerse, E. *Chem. Rev.* **2014**, 4081-4148. (c) Schilter, D.; Camara, J. M.; Huynh, M. T.; Hammes-Schiffer, S.; Rauchfuss, T. B. *Chem. Rev.* **2016**, 8693-8749.

NUEVAS METODOLOGÍAS SINTÉTICAS BASADAS EN ALENOS, ALQUINOS Y HETEROCICLOS BIOACTIVOS

B. Alcaide[1], P. Almendros[2], I. Burgos[1], E. Busto[1].

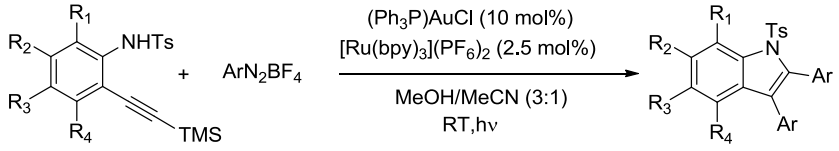
[1]*Grupo de Lactamas y Heterociclos Bioactivos, Departamento de Química Orgánica I, Unidad Asociada al CSIC, Facultad de Química, Universidad Complutense de Madrid, Madrid, Spain;* [2]*Instituto de Química Orgánica General, CSIC, Madrid, Spain.*

iburgos@ucm.es

Keywords*: catalysis, photoredox, indoles.*

Homogeneous catalysis using gold salts has been developed as a powerful tool in the field of synthetic organic chemistry. Particularly attractive is the activation of alkenes, alkynes and allenes by cationic gold species (I). [1] However, Au (I) / Au (III) catalytic cycles cannot be accessed through traditional processes catalyzed with Au (I), and stoichiometric or higher amounts of a strong oxidant are required to exceed the high potential of the Au (I) / Au (III) redox pair. [2] Glorius and Toste independently developed an intelligent strategy to avoid the disadvantage of the inclusion of strong oxidants, [3] by the use of a photo-redox catalyst and a diazonium salt. [4]

The synthesis of 2,3-disubstituted indoles has been carried out using aminoalkynes and diazonium salts as starting materials. This synthesis was accomplished by means of a photoredox reaction using two catalysts, a Au (I) salt and a ruthenium Ru (II) complex under conditions previously optimized by the research group where the project was carried out.



To probe the versatility of the photoredox reaction, a set of examples has been synthesized, including a broad spectrum of functional groups with different electronic properties (strongly electron withdrawing groups, weakly electron withdrawing groups, weakly electron donor groups).

References:

[1] Joost M.; Amgoune A.; Bourissou D. *Angew. Chem.* **2015**, *127*, 15234.

[2] Cresswell A. J.; Lloyd-Jones G. C. *Chem. Eur. J.* **2016**, *22*, 12641.

[3] Sahoo B.; Hopkinson M. N.; Glorius F. *J. Am. Chem. Soc.* **2013**, *135*, 5505.

[4] Hopkinson M. N.; Sahoo B.; Glorius F. *Adv. Synth. Catal.* **2014**, *356*, 2794

Dynamic Combinatorial Chemistry driven by proteins and applied to drug discovery

A. Canal-Martín[a], J. Sastre[a], C. Roca[a], M. J. Sánchez-Barrena[b], Á. Canales[c], F. J. Cañada[a], J. Jiménez-Barbero[d], A. Martínez[a], R. Pérez-Fernández [a]

[a] *Chemical and physical biology department, Centro de Investigaciones Biológicas, CIB-CSIC, Madrid 28040, Spain.*
[b] *Crystallography and structural biology department, Instituto de Química Física Rocasolano, IQFR-CSIC, Madrid 28006, Spain.*
[c] *Organic chemistry department, Universidad Complutense de Madrid, Madrid 28040, Spain.*
[d] *Molecular recognition and host-pathogen interactions, CIC bioGUNE, Derio 48160, Bizkaia, Spain.*

e-mail: andreacm26@hotmail.com

Keywords: *Dynamic Combinatorial Chemistry, Frequenine-2, Fragil X Syndrome.*

The development of synthetic molecules that mimics the precision of nature in molecular recognition represents a huge challenge to chemists. Dynamic combinatorial chemistry (DCC) holds enormous potential for drug discovery speeding the identification and optimization of novel ligands for biological targets. In DCC, building blocks react with one another using reversible chemical reactions giving mixtures of oligomers (Dynamic combinatorial libraries, DCLs). If a protein is added to the system and one or more molecules show affinity to it, these building blocks will, according to the Le Chatelier's principle, be amplified on the expense of the other non-bonding constituents. (**Fig.1**) [1]

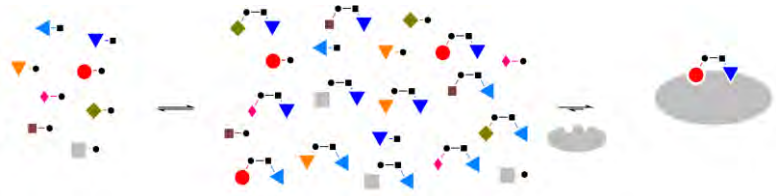


Fig. 1. Dynamic combinatorial chemistry with protein as template

We present the discovery of novel ligands of Frequenine-2 (Frq2), a high-affinity Ca^{2+}binding protein conserved from yeast to humans (named Neuronal Calcium Sensor-1). Frq2 is involved in pathologies that result from an abnormal synapse number such as Fragile X syndrome (FXS).[2] Fragile X syndrome is the most common inherited cause of intellectual disability and a common known single gene cause of autism spectrum disorders. [3]

References:

[1] (a) Corbett, P. T.; Leclaire, J.; Vial L.; West, K. R.; Wietor, J. L.; Sanders, J. K. M.; Otto, S. *Chem. Rev.* **2006,** *106*, 3652. (b) Mondal, M.; Hirsch, A. K. H. *Chem. Soc. Rev.* **2015,** *44,* 2455.
[2] Sastre, A.; Campillo, N. E.; Gil, C.; Martínez, *A. Curr. Opin. Behav. Sci.* **2015**, *4*, 6.
[3] Mansilla, A.; Chaves-Sanjuan, A.; Campillo, N. E.; Semelidou, O.; Martínez González, L.; Infantes, L.; González-Rubio, J. M.; Gil, C.; Conde, S.; Skoulakis, E. M. C.; Ferrús, A.; Martínez, A.; Sánchez-Barrena, M. J. *Proc. Natl. Acad. Sci. USA* **2017,** *114*, E999.

Nueva síntesis de análogos de la vitamina D con unidad carboránica en la cadena lateral

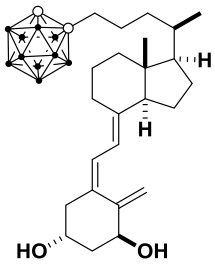
N. Carballo Pedrares, R. Sigüeiro, A. Mouriño

Laboratorio Ignacio Ribas. Dpto. de Química Orgánica. Facultad de Química. Universidad de Santiago de Compostela.
e-mail: nataliacarballo129@gmail.com

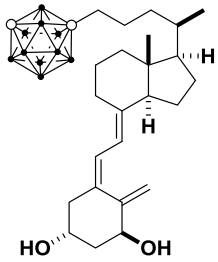
***Keywords**: Vitamin D nuclear receptor, carborane, drug discovery.*

Recientemente Otero y *col*. publicaron el diseño, síntesis y evaluación biológica de un nuevo análogo de la 1α,25-dihidroxivitamina D_3 (calcitriol) que posee un *orto*-carborano en su cadena lateral. En la estructura cristalográfica del complejo formado por el análogo carboránico **1** y el VDR (*Receptor nuclear de la vitamina D*), la unidad carboránica mimetiza la interacciones del C25-OH del calcitriol con las histidinas His333 y His423 del zVDR. Aunque no es posible discernir la naturaleza de las interacciones entre la unidad carboránica y estas histidinas, debido a que la técnica de difracción de RX no es capaz de localizar la posición de los hidrógenos, en este articulo se postula que dichas interacciones son de enlaces de dihidrógeno (B-H···H-N) inusuales.[1]

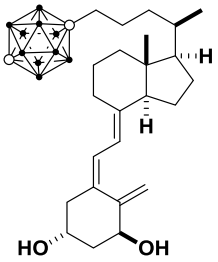
El presente proyecto consistió en el desarrollo de una nueva ruta de síntesis del análogo **1**, que posibilita la obtención de los análogos **2** y **3**, correspondientes a los isómeros *meta* y *para*-carboránicos. Además, la resolución de las estructuras cristalográficas de los complejos formados entre estos análogos y el VDR permitirá confirmar si las interacciones son mediante enlaces de dihidrógeno y averiguar si existen diferencias entre las propiedades biológicas de los isómeros *orto*-, *meta*- y *para*-carboránicos.



1 (*orto*)



2 (*meta*)



3 (*para*)

References:

[1] Otero, R.; Seoane, S.; Sigüeiro, R.; Belorusova, A.Y.; Maestro, M.A.; Pérez-Fernández, R.; Rochel, N.; Mouriño, A. *Chem. Sci.* **2016**, *7*, 1033-1037.

Palladium catalyzed formal (5+2) annulation between *o*-alkenylanilides and allenes

Borja Cendón,[1] Noelia Casanova,[1] Cezar Comanescu,[2] Rebeca García-Fandiño,[3] Andrés Seoane,[1] José Luis Mascareñas,[1] Moisés Gulías.[1]

[1] *Centro Singular de Investigación en Química Biológica y Materiales Moleculares (CIQUS), C/ Jenaro de la Fuente s/n 15782 Santiago de Compostela, A Coruña, Spain.*

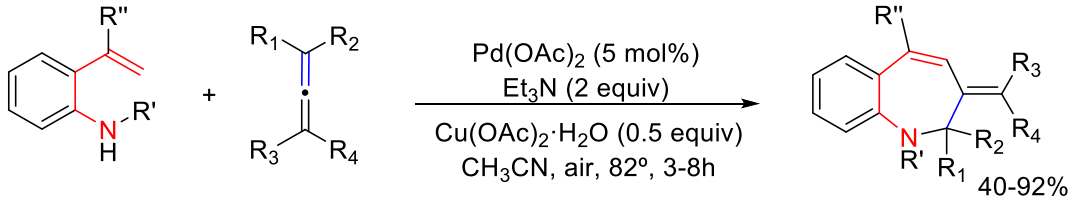
[2] *Department of Inorganic Chemistry, University Politehnica of Bucharest, 1, Polizu st., RO-011061 Bucharest, România.*

[3] *CIQUP, R. Campo Alegre s/n, P-4169-007, Porto, Portugal.*

borja.cendon.marino@usc.es

***Keywords**: C-H activation, benzazepine, cycloaddition*

During the past years our group has been studying the novel reactivity of o-alkenylphenols towards Rh(III) and Pd(II)-catalyzed C-H annulations with alkynes and allenes.[1] Herein we disclose an extension of our previous work by replacing the -OH of the phenol for an appropppriately substituted amine which reacts with allenes upon treatment with catalytic amounts of Pd(OAc)2 and Cu(II) to give highly valuable 1H-benzo[b]azepines, in good yields, and with very high regio- and diastereoselectivities, by a formal (5+2) cycloaddition.[2]
In this communication we describe the influence of substituents on the nitrogen in the efficiency of the reaction and in the formation of side products such as indole or indoline. Furthermore, we demostrate that yields are considerably increased in the presence of triethylamine. We also study the scope of the reaction with different anilides and allenes and propose a mechanistic hypothesis for this transformation, supported by DFT calculations, which suggest that the C-H activation of the alkenylanilide involves a classical CMD mechanism.



[1] (a) Seoane, A.; Casanova, N.; Quiñones, N.; Mascareñas, J. L.; Gulías, M. *J. Am. Chem. Soc.* **2014**, 136, 7607. (b) Seoane, A.; Casanova, N.; Quiñones, N.; Mascareñas, J. L.; Gulías, M. *J. Am. Chem. Soc.* **2014**, 136, 834. (c) Casanova, N.; Del Rio, K. P.; García-Fandiño, R.; Mascareñas, J. L.; Gulías, M. *ACS Catal.* **2016**, 6, 3349. (d) Casanova, N.; Seoane, A.; Mascareñas, J. L.; Gulías, M. *Angew. Chem., Int. Ed.* **2015**, 54, 2374.
[2] Cendón, B.; Casanova, N.; Comanescu, C.; García-Fandiño, R.; Seoane, A.; Gulías, M.; Mascareñas, J.L. *Org. Lett.*, **2017**, 19, 1674.

REACTIVIDAD DIVERGENTE ENTRE CICLOPROPENONAS Y α-IMINOÉSTERES DEPENDIENTE DEL CATALIZADOR

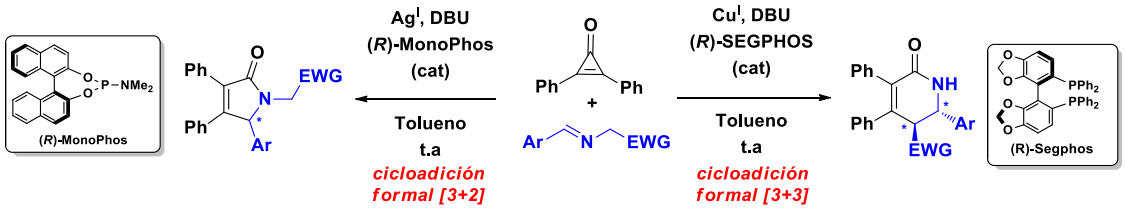
Javier Corpas, Alberto Ponce, Javier Adrio*, Juan C. Carretero*.

Departamento de Química Orgánica, Universidad Autónoma de Madrid. Cantoblanco, 28049 Madrid.
e-mail: *javier.corpas@estudiante.uam.es*

Palabras clave: *catálisis asimétrica, ciclopropenonas, reacciones de cicloadición, iluro de azometino.*

Las ciclopropenonas son motivos estructurales versátiles en síntesis orgánica debido a las propiedades electrónicas que presentan, siendo uno de los sistemas monocíclicos con aromaticidad de Hückel más pequeños. Desde un punto de vista sintético son sintones 3C interesantes debido a sus propiedades anfifílicas, ya que pueden reaccionar fácilmente con electrófilos o nucleófilos [1]. En este sentido presentan un elevado interés como dipolarófilo en reacciones de cicloadición 1,3-dipolar, propiedad que puede exhibir a través del enlace C=C o bien del C=O [2], así como 1,3-dipolos cuando existe una activación previa de la misma por parte de una base de Lewis [3].

En este trabajo se estudia la reacción entre ciclopropenonas y α-iminoésteres, en combinación con cantidades catalíticas de complejos de metales de transición en presencia de una base. Los resultados obtenidos hasta el momento muestran una reactividad divergente dependiente del sistema catalítico utilizado. Al emplear complejos de Cu^{I}/difosfina la reacción transcurre sobre el enlace C=O del anillo de ciclopropenona, conduciendo a la formación de lactamas de seis miembros mediante un proceso de cicloadición formal [3+3]. Por otro lado, al emplearse complejos de Ag^{I} con fosforamiditos se ha observado que la reacción transcurre mediante una cicloadición formal [3+2], obteniéndose la lactama de cinco miembros.



Referencias:

[1] K. Komatsu, T. Kitagawa, *Chem. Rev*. **2003**, 103, 1371.

[2] (a) R. A. Pilli, J. A. R. Rodrigues, A. Kascheres, *J. Org. Chem.*, **1983**, *48*, 1084. (c) A. R. Rivero, I. Fernández, C. R. de Arellano, M. A. Sierra, *J. Org. Chem*. **2015**, 80, 1207. (d) F. Xie, S. Yu, Z. Qi, X. Li, *Angew. Chem. Int. Ed.* **2016**, *55*, 15351.

[3] J. Xu, J. Cao, C. Fang, T. Lu, D. Du, *Org. Chem. Front.* **2017**, 4, 560.

Desarrollo de nuevas glicoestructuras derivadas del ácido glucurónico con actividad frente a infecciones del virus del Dengue

V. Fernández Cabello

Estudiante del Máster Universitario de Química Orgánica, Departamento de Química Orgánica, Facultad de ciencias, Universidad Autónoma de Madrid, España
e-mail: victor.fernandezc@estudiante.uam.es

***Keywords**: virus del Dengue, Glicomimético, Ácido glucurónico*

Abstract: En el presente trabajo se plantea la síntesis de varios glicomiméticos derivados del ácido glucurónico. Se ha realizado la síntesis del ácido glucurónico funcionalizado en la posición anomérica con una cadena alquílica y un grupo azida[1]. Igualmente se han preparado 3 "cores" con diferente grado de multivalencia, es decir, con 2, 3 y 4 grupos etinilo terminales[2]. La posterior formación de un linker triazol mediante "click chemistry" entre el resto azida del glicósido y los grupos etinilo de los "cores" permite la obtención de diversos compuestos, estructuralmente parecidos y capaces de simular a los glicósidos presentes en la membrana celular[2] (glicomiméticos), con posible actividad terapéutica frente al virus del Dengue.

Referencias:

[1] Chen, Y.; Li, Y.; Yu, H.; Sugiarto, G.; Thon, V.; Hwang, J.; Ding, L.; Hie, L.; Chen, X. *Angew. Chem. Int. Ed.* **2013**, *52*, 11852-11856.

[2] C. Bayón, N. He, M. Deir-Kaspar, P. Blasco, S. André, H.-J. Gabius, Á. Rumbero, J. Jiménez-Barbero, W.-D. Fessner, M. J. Hernáiz, *Chem. Eur. J.* **2017**, 23, 1623.

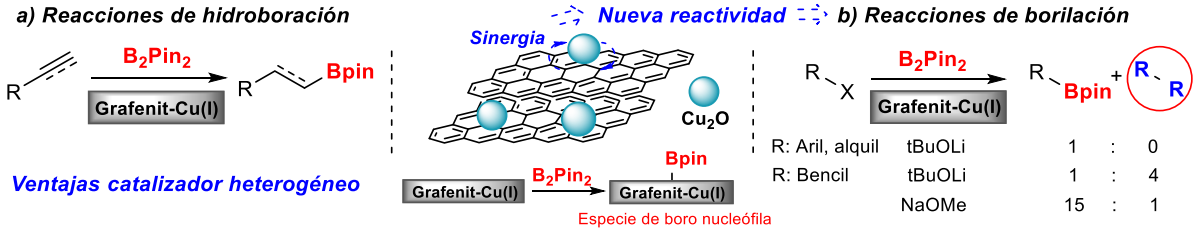
Empleo de catalizadores heterogéneos de cobre soportados en grafeno en la formación de enlaces C-C y C-B

M. Franco Fernández, B. Cid de la Plata, M. Tortosa Manzanares.

Departamento de Química Orgánica, Universidad Autónoma de Madrid
e-mail: mario.franco@estudiante.uam.es

***Keywords**: Catálisis heterogénea, Boro, Grafeno.*

El crecimiento de la química verde en los últimos años ha conducido al desarrollo de técnicas cada vez más sostenibles, siendo una de las más importantes el empleo de catalizadores heterogéneos, los cuales presentan baja toxicidad, fácil manejo y reutilización.[1] En este contexto, se ha desarrollado en el grupo de investigación un catalizador de Cu(I) soportado sobre nanoplaquetas de grafeno **(Grafenit-Cu(I))**.[2] Debido a la importancia, versatilidad y amplio campo de aplicación de compuestos borilados, el presente trabajo se centra en el estudio del comportamiento del **Grafenit-Cu(I)** en reacciones de formación de enlaces C-B.
Se han analizado diferentes tipos de *reacciones de hidroboración* de sistemas insaturados (a) y de *borilación* de diferentes haluros (b), obteniendo en cada caso los correspondientes ésteres borónicos con las ventajas intrínsecas mencionadas de un catalizador heterogéneo. El hecho más destacable es que, en el caso de los haluros bencílicos, según las condiciones de reacción se puede obtener selectivamente bien el producto de homoacoplamiento (R-R) por formación de enlace C-C o el esperado de borilación.



Este tipo de procesos de homoacoplamiento se ha observado con catalizadores de niquel[4] pero no se ha estudiado con catalizadores de cobre. Hemos comprobado que esta nueva reactividad, de elevado potencial sintético, se debe al efecto sinérgico entre el Cu_2O y la lámina de grafeno. Esta interacción confiere unas propiedades diferentes al Cu_2O y aporta un valor añadido al material explorado como catalizador heterogéneo.

Referencias:

[1] Hübner, S.; de Vries, J. G.; Farina, V. *Adv. Synth. Catal.* **2016**, *358*, 3–25.
[2] Triminì, A. Preparation an analysis of the catalytic activity of copper oxide nanoparticles supported on graphene nanoplatelets. M. S. Thesis, Universidad Autónoma de Madrid, Madrid, 2015.
[3] Marder, T. B.; Westcott, S. A.; Mkhalid, I. A.; Geirer, S. J.; Neeve, E. C. Chem. Rev. **2016**, *116*, 9091-9161.
[4] Gong, H.; Deng, W.; Qian, Q.; Zhao, C.; Xu, H. *Chem. Sci.* **2013**, *4*, 4022-4029.

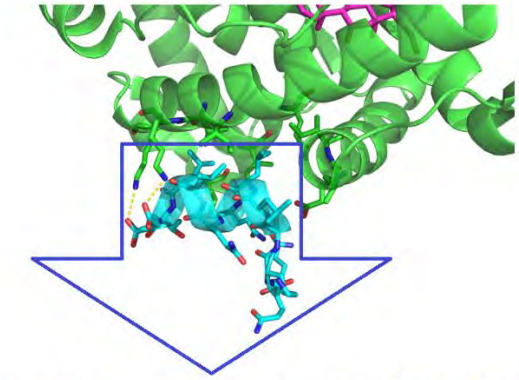
LINEAR AND CYCLIC (10-12)-MER PEPTIDES AS MINERALOCORTICOID RECEPTOR MODULATORS

J. Garcés Garcés, Mª. J. Pérez de Vega

Instituto de Química Médica-CSIC, Madrid, Spain
jgarces@ucm.es

***Keywords**: Mineralocorticoid receptor, solid phase synthesis, peptides*

The mineralocorticoid receptor (MR) belongs to the nuclear receptor family, and plays a key role on the regulation of the hemodynamic and electrolytic homeostasis, therefore, it constitutes an important therapeutic target for the treatment of cardiovascular pathologies.[1] The biological activity of MR is mediated by the interaction with its endogenous ligands, mainly aldosterone, which in turn favors the interaction with coactivators, like the SRC1.The coactivators interact with the MR through helical regions that contain the key motifs LXXLL. Several studies have shown that the sequence SRC1-4 is this that shows a higher affinity for the MR.[2] In this context, our project is aiming to block the MR-coactivator interaction with the final objective of hindering the MR biological action. Thus, linear and cyclic peptides containing the motif LXXLL have been designed based on a fragment of the coactivator SRC1-4, with the aim of disrupting the interaction MR-SRC1-4. The peptides were synthesized following solid phase synthesis protocols. Conformational studies by circular dichroism will be performed to check the helical conformation of the peptides.



SRC1-4: Gln-Gln-Lys-Ser-Leu-Leu-Gln-Gln-Leu-Leu-Thr-Glu

Analogues to SRC1-4

Ac-Gln-Gln-Lys-Ser-Leu-Leu-Glu-Gln-Leu-Leu-Lys-Glu-NH_2

Ac-Gln-Gln-Lys-Ser-Leu-Leu-Glu-Gln-Leu-Leu-Lys-Glu-NH_2
CO—NH

Ac-Lys-Ser-Leu-Leu-Glu-Gln-Leu-Leu-Lys-Glu-NH_2

Ac-Lys-Ser-Leu-Leu-Glu-Gln-Leu-Leu-Lys-Glu-NH_2
CO—NH

[1] Lifton, R. P.; Gharavi, A. G.; Geller, D. S. *Cell* **2001**, *104*, 545-556.
[2] Needham, M,: Raines, S.; McPheat, J.; Stacey, C.; Ellston, J.; Hoare, S.; Parker, M. *J. Steroid. Biochem. Mol. Biol*. **2000**, *72*, 35-4

This work was supported by the Spanish Ministerio de Economía y Competitividad, Plan Nacional SAF2015-66275-C2-2-R.

Reacciones de funcionalización C–H catalizadas por Pd

B. González-Blázquez, M. T. Quirós, D. J. Cárdenas

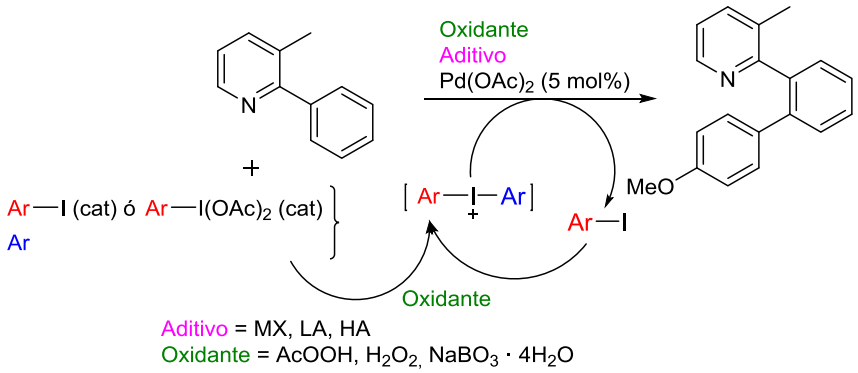
Departamento de Química Orgánica, Facultad de Ciencias, Universidad Autónoma de Madrid
e-mail: borja.gonzalezb@estudiante.uam.es

***Palabras clave**: arilación C–H, yodo hipervalente, paladio*

Las reacciones de funcionalización C–H[1] (en concreto arilación C–H) catalizadas por metales de transición están siendo objeto de estudio en los últimos años debido a su importancia, ya que permiten hacer las síntesis más eficientes, rebajar costes, etc. El metal que ha dado mejores resultados en este tipo de reacciones es el paladio.

Para llevar a cabo estas reacciones pueden utilizarse diferentes agentes arilantes, en nuestro caso nos centraremos en las sales de diarilyodonio,[2] compuestos hipervalentes de yodo(III). En este proceso se libera como subproducto un equivalente de yodoareno, lo que es indeseable desde el punto de vista de la química verde, debido a su baja economía atómica y su toxicidad.

Por ello, en este trabajo se estudia la reacción de arilación C–H de un derivado de piridina[3] generando *in situ* la sal de diarilyodonio a partir del yodoareno, el grupo arilo que se quiere transferir y un oxidante, todo ello en medio ácido. Se pretende optimizar el proceso utilizando el yodoareno en cantidad estequiométrica para después, aprovechando su liberación como subproducto en el medio de reacción, reducir su uso a cantidades catalíticas, con lo que se reduciría la cantidad de yodoareno necesario y su gasto como subproducto de reacción.



Referencias:

(1) Lyons, T. W.; Sanford, M. S. *Chem. Rev.* **2010**, *110*, 1147-1169.

(2) Merritt, E. A.; Olofsson, B. *Angew. Chem. Int. Ed.* **2009**, *48*, 9052-9070.

(3) Deprez, N. R.; Sanford, M. S. *J. Am. Chem. Soc.* **2009**, *131*, 11234-11241.

Silicon Dienolate Addition to Isatins Employing Bifunctional Catalysts

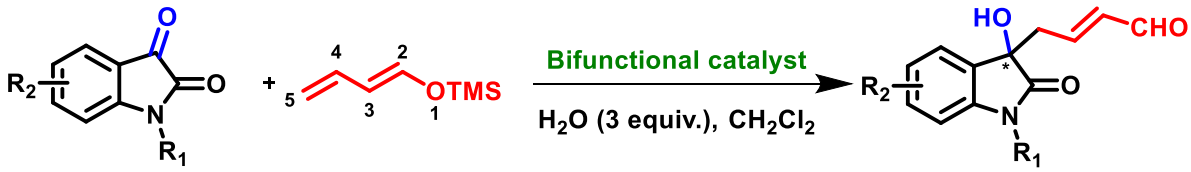
J. Humbrías Martín, J. Alemán, J. A. Fernández

Departamento de Química Orgánica (L305 – Módulo 02),
Universidad Autónoma de Madrid, Cantoblanco, 28049, Madrid
e-mail: jorge.humbrias@estudiante.uam.es

***Keywords**: organocatalysis, asymmetric synthesis, vinylogous Mukaiyama aldol reaction, isatin.*

The aldol reaction is a powerful tool to form new C-C bonds. Since its discovery in 1872, there have been countless modifications and studies to solve the selectivity problems associated with its use in the first attempts. The aldol Mukaiyama reaction appeared to solve these selectivity issues, becoming an improved version of the traditional aldol reaction.[1] During the past century, a plethora of new studies about the aldol Mukaiyama reaction have been reported in the literature, including for instance the use of vinylogous enolates.[2] Due to the importance of synthesizing enantiomerically pure compounds, new asymmetric Mukaiyama methodologies (by using a variety of chiral catalysts) have been developed during the last decades.[3]

Last year, our research group found a completely new reactivity for vinylogous enolates.[4] In the presence of a bifunctional organocatalyst (based on thioureas or squaramides with tertiary amines) and facing nitro alkenes as electrophiles, dienolates were found to react through the 3 position instead of the more reactive 5 position. Herein, we describe a new enantioselective vinylogous aldol Mukaiyama addition to isatin, which is an interesting scaffold found in natural products and biologically active compounds, using bifunctional organocatalysts.



References:

[1] Mukaiyama, T.; Narasaka, K.; Banno K. *Chem. Lett.* **1973**, 1011-1014.

[2] Kalesse, M.; Cordes, M.; Symkenberg, G.; Lu H. *Nat. Prod. Rep*. **2014**, *31*, 563-594.

[3] Matsuo, J.; Murakam, M. *Angew. Chem. Int. Ed.* **2013**, 52, 9109-9118.

[4] Frias, M.; Mas-Balleste, R.; Arias, S.; Alvarado, C.; Aleman, J. *J. Am. Chem. Soc.* **2017**, *139*, 672-679.

Study of the structural requirements for the transposition of iodine in aryl phosphonates

Javier López Martínez, Miguel A. Sierra, Roberto Martínez-Álvarez

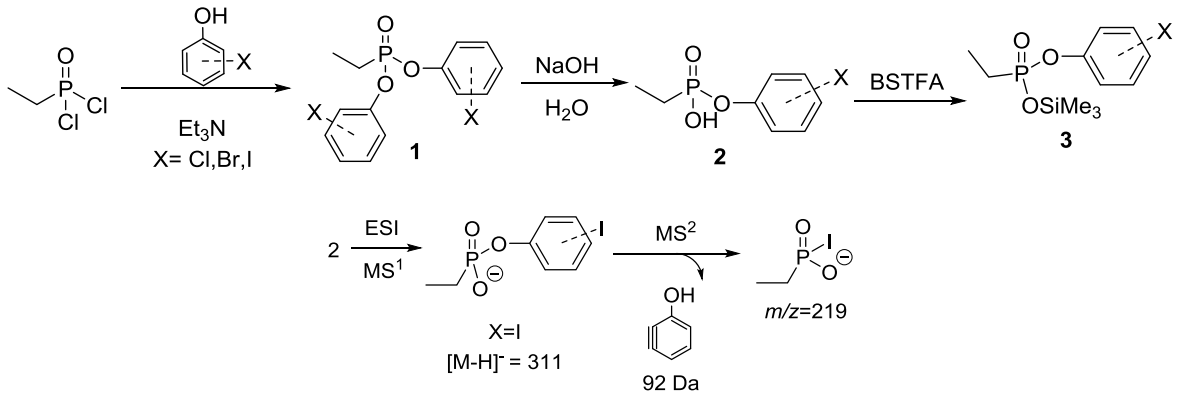
Departamento de Química Orgánica I, Facultad de Ciencias Químicas, Universidad Complutense de Madrid, 28040 Madrid (Spain). Centro de Innovación en Química Avanzada (ORFEO-CINQA), Facultad de Ciencias Químicas, Universidad Complutense de Madrid.

e-mail: javlop03@ucm.es

***Keywords**: phosphonates, mass spectrometry, halogen rearrangement*

The study by mass spectrometry of different halogenated alkyl phosphonates has shown that under these conditions an iodine atom migration takes place similarly to the well-known McLafferty rearrangement.[1]
In order to determine the structural requirements for this migration, we have studied the mass spectra of halogenated arylphosphonates. The synthesis of diaryl phosphonates is carried out by reaction of ethylphosphonic dichloride with 2, 3 and 4-halogenated phenols (Cl, Br, I) in presence of a base.[2] The corresponding monoesters are obtained by basic hydrolysis of the diesters. The mass spectra of the corresponding diesters have been recorded under EI while the mass spectra of monoesters were obtained under ESI conditions. Finally, the mass spectra of monoesters were also recorded under EI after the corresponding derivatization with BSTFA.

The preliminary results indicate that the iodinated monoarylposphonates undergo an elimination of a neutral molecule (92 Da). This fragmentation can be only explained assuming an intramolecular migration of an iodine atom.



[1]. Picazas-Marquez, N.; Sierra, M.; Nova, C.; Manuel Moreno, J.; Aboitiz, N.; de Rivas, G.; Sierra, M. A.; Martinez-Alvarez, R.; Gomez-Caballero, E. *J. Am. Soc. Mass Spectrom.* **2016**, *27*, 1510-1519.
[2].McWhirter, C.; Lund, E. A.; Tanifum, E. A.; Feng, G.; Sheikh, Q. I.; Hengge, A. C.; Williams, N. H. *J. Am. Chem. Soc.* **2008**, *130*, 13673-13682.

Sintesis de γ-aminoácidos funcionalizados en la posición C2 o Beta

Francisco Molina, Manuel Amorín, Juan R. Granja

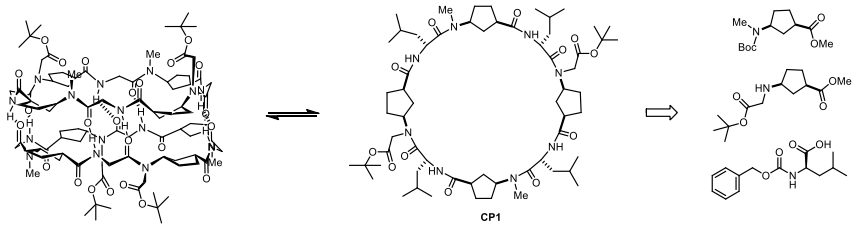
Departamento de Química Orgánica Y Centro Singular de Investigación en Química Biológica y Materiales moleculares (CIQUS). Campus Vida. Universidad de Santiago de Compostela. 15782 Santiago de Compostela, España.

francisco.molina@rai.usc.es

***Keywords**: ciclopéptido, nanoestructura, síntesis*

En los últimos años, ha habido un gran avance en el campo de la nanotecnología por lo que existe un gran interés en la obtención de nuevos tipos de nanoestructuras en las que se pueda conseguir un estricto control topológico. En la década de los 90 se prepararon lo primeros nanotubos ciclopeptídicos,[1] y estos han demostrado ser una herramienta muy versátil en este campo. Nuestro grupo ha desarrollado un nuevo tipo de ciclopéptidos compuestos por α y γ-aminoácidos,[2] en los que se puede modificar su nitrógeno amidíco para formar dímeros estables que presenten grupos funcionales en la vertical del anillo.

En esta comunicación se presenta la síntesis de un α,γ-ciclooctapeptido funcionalizado con dos ácidos carboxílicos. Se han utilizado dos γ-aminoácidos derivados del acp, funcionalizados mediante la estrategia de Fukuyama;[3] uno conteniendo un grupo metilo y otro un grupo acido protegido (acetato de terbutilo). Para la síntesis peptídica se ha optado por una estrategia altamente convergente en disolución debido a la alta simetría del ciclopéptido.



References:
[1] Ghadiri, M. R.; Granja, J. R.; Milligan, R. A.; McRee, D. E.; Khazanovich, N. *Nature* **1993**, *366*, 324-327.
[2] Amorín. M.; Castedo, L.; Granja, J.R. *J. Am. Chem. Soc.* **2003**, *125*, 2844-2845.
[3] T. Kan, T. Fukuyama, *Chem. Commun.* **2004**, 353-359

Procesos catalizados por Fe para la formación de enlaces C-C y C-B

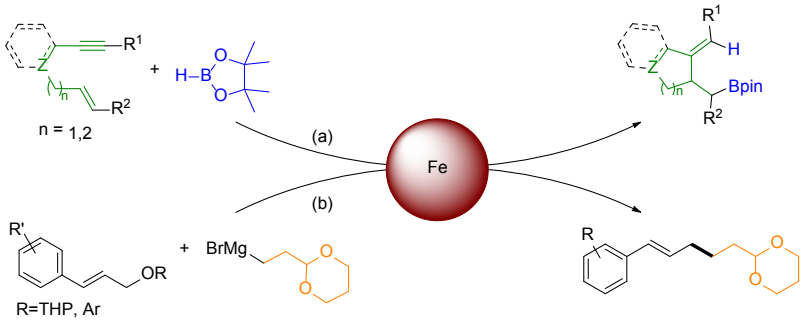
J. C. Nieto Carmona, N. Cabrera, G. Caballero, D. J. Cárdenas, E. Buñuel

Departamento de Química Orgánica, Facultad de Ciencias, Universidad Autónoma de Madrid
e-mail: juanc.nieto@estudiante.uam.es

***Palabras clave**: hierro, acoplamiento cruzado, ciclación borilativa*

A lo largo de los últimos años, el empleo de metales de la primera serie de transición ha permitido el desarrollo de nuevos procesos catalíticos más respetuosos con el medioambiente, debido a su menor coste y a su baja toxicidad, desplazando así a otros metales más utilizados, tales como Pd, Pt, Ru o Rh. Entre estos metales, el Fe está adquiriendo una gran importancia ya que muestra una elevada versatilidad. Además, el estudio de su papel en procesos catalíticos, donde se ponen en juego mecanismos todavía inexplorados, resulta muy atractivo.

En este trabajo se abordan dos procesos catalizados por complejos de Fe dirigidos hacia la formación de enlaces C-C y C-B. Por un lado, tomando como precedente la reacción de ciclación borilativa catalizada por Pd desarrollada en nuestro grupo,[1] se investiga su extensión y mejora en procesos catalizados por Fe (Ruta a). El interés de esta línea reside en la capacidad para formar simultáneamente uno o varios enlaces C-C y C-B, lo que conduce de manera sencilla a la obtención de boronatos estructuralmente complejos y de gran utilidad sintética. Por otro lado, se está explorando la reacción de sustitución alílica de éteres con reactivos de Grignard catalizada por Fe (Ruta b). En este caso, con el fin de superar las dificultades encontradas en este tipo de procedimientos,[2] nuestros esfuerzos se centran en la formación de enlaces C(sp^3)-C(sp^3). Además de los beneficios que aporta el empleo de complejos de Fe no tóxicos como catalizadores, la principal ventaja frente a otras reacciones de sustitución alílica consiste en el empleo de sustratos estables, no activados y no tóxicos.



Referencias:

[1] E. Buñuel, D. J. Cárdenas *Eur. J. Org. Chem.* **2016**, 5446.

[2] L. Qi, E. Ma, F. Jia, Z. Li, *Tetrahedron Lett.* **2016**, *57*, 2211.

Synthesis of Metal-Salen Complex with a Pair of Nucleosides Attached by Click Chemistry

Pablo Ortega,[a,b] María del Carmen Pérez,[a,b] Luis Casarrubios,[a,b] Mar Gómez-Gallego,[a,b] Miguel A. Sierra[a,b]

[a] *Departamento de Química Orgánica I, Facultad de Ciencias Químicas, Universidad Complutense de Madrid, 28040 Madrid (Spain)*
[b] *Centro de Innovación en Química Avanzada (ORFEO – CINQA), Universidad Complutense de Madrid, 28040 Madrid (Spain)*

p.ortega@ucm.es

***Keywords**: Metal-Salen complex, Click chemistry, Nucleosides*

The discovery of new metallated complexes which own useful properties in terms of photoactivity, selectivity, biological or pharmacological activity is an important research field in actual chemistry. Moreover, the synthesis of nucleosides attached to these metallated complexes has allowed the development of new drugs with antiviral, antifungical, antibacterial and antimicrobial activity.[1] In this field, our research group has previously published the synthesis of metallo-nucleosides and the study of their reactivity and their incorporation of fluorescent and redox labels in their structures.[2]

Herein, we report the cycloaddition catalyzed by Cu(I) between an unnatural nucleoside bearing an azide moiety and an alkynilated salicylaldehyde,.[3] Thus, the reaction of the obtained molecules with a cationic metal M and o-phenylendiamine leads to a metal-Salen complex. We also report the study of it photochemical and redox properties.

M= Cu(II), Fe(II), Mn(II), Ni(II), Zn(II)

[1] Saini, A. K.; Kumari, P.; Sharma, V.; Mathur, P.; Shaikh, M.M. *Dalton Trans.*, **2016**, *45*, 19096-19108.
[2] a) Valencia, M.; Martín-Ortiz, M.; Gómez-Gallego, M.; Ramírez de Arellano, C.; Sierra, Miguel A. *Chem. Eur. J.* **2014**, *20,* 3831-3838; b) Martin-Ortiz, M.; Gómez-Gallego, M.; Ramírez de Arellano, C.; Sierra, M. A. *Chem. Eur. J.* **2012**, *18,* 12603-12608.
[3] Casarrubios, Luis; de la Torre, Maria C.; Sierra, Miguel A. *Chem. Eur. J.* **2013**, *19*, 3534-3541.

Bioorthogonal catalysis with ruthenium complexes

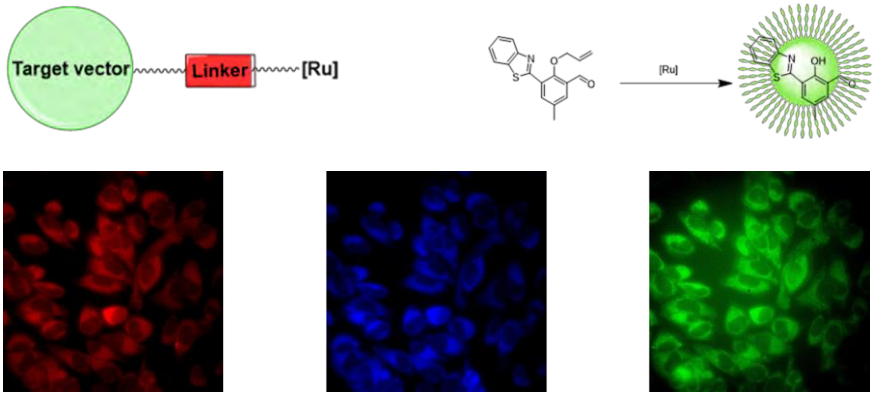
Sandra Rodríguez Álvarez [a], María Tomás Gamasa [a] and José Luis Mascareñas Cid [a]

[a] *Dpto. De Química Orgánica, Centro de Investigaciones en Química Biológica y Materiales Moleculares (CIQUS), Universidad de Santiago de Compostela, 15782.*
e-mail: sandra.rodriguez.alvarez@rai.usc.es

***Keywords**: Bioorthogonal catalysis, ruthenium and living cells.*

The study of biomolecules in their natural environment has been an object of interest in science over the years. The concept of bioorthogonal chemistry is based on the development of chemical reactions that do not generate adverse effects in biological systems. Albeit yet in its total infancy, recent works have demonstrated the viability of intracellular metal catalysis.[1,2]

Previous work of our group demonstrate that is possible to generate artificial catalytic power and fluorescent imaging in a specific cellular organelle, such as the mitochondria.[3] Now, we report here the design and development of a new generation of ruthenium complexes that also target the mitochondria and are capable of promoting a localized bioorthogonal catalytic reaction inside this organelle.



These new and specific catalysts are composed of a ruthenium complex, a liphophylic linker, a phosphonium group which is an adequate mitochondria target vector and a pyrene fluorescent unit. We show here that these catalysts not only present blue fluorescence, but also can promote the uncaging of allyl-protected alcohols in mammalian cells such as HeLa cells. In addition, these new ruthenium complexes not only are well internalized, but also accumulate in mitochondria and present a higher intensity of fluorescence than the previous catalysts.

[1] Yusop, R. M.; Unciti-Broceta, A.; Johansson, E. M.; Sanchez-Martin, R. M.; Bradley, M. *Nature Chem.* **2011**, *3*, 239.
[2] Völker, T.; Dempwolff, F.; Graumann, P. L.; Meggers, E. *Angew Chem Int Ed Engl.* **2014**, *53*, 10536.
[3] Tomás-Gamasa, M., Martínez-Calvo, M., Couceiro, J. R., Mascareñas, J. L., *Nat. Commun.* **2016**, *7*, 12538.

NEW SYNTHETIC METHODOLOGIES BASED IN ALLENES, ALKYNES AND BIOACTIVE HETEROCYCLES

Guillermo Palop,[a] Benito Alcaide,[a] Pedro Almendros[b] and Teresa Martínez del Campo[a]

[a]*Grupo de Lactamas y Heterociclos Bioactivos, Departamento de Química Orgánica, Unidad Asociada al CSIC, Facultad de Química, Universidad Complutense de Madrid, 28040-Madrid;* [b] *Instituto de Química Orgánica General, IQOG, CSIC, Juan de la Cierva 3, 28006-Madrid.*

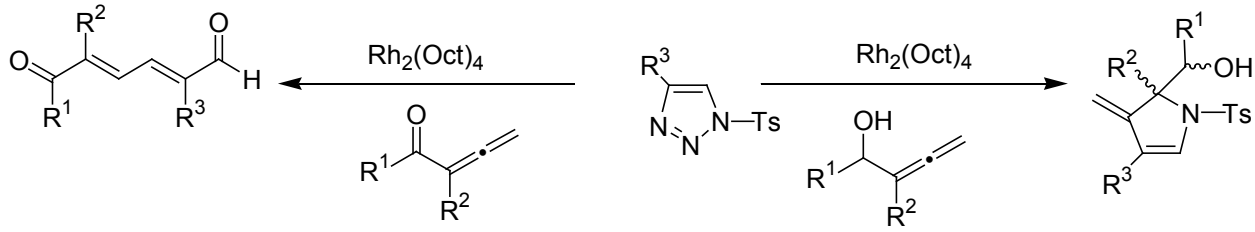
gpalop@ucm.es

Keywords: *(triazole, allenol, allenone)*

4-Substituted 1-sulfonyl-1,2,3-triazoles act as precursors for reactive transitions metal complexes of α-imino carbenes.[1] The nitrogen atom of the α-imino group is a nucleophile and could participate in cycloaddition reactions with unsaturated compounds to construct *N*-heterocycles.

On the other hand, allenes have metamorphosed from a curiosity to a versatile and uniquely reactive functional group, allowing chemists to prepare a variety of compounds of chemical and biological interest.

In continuing with our interest in metal-catalysed processes and allene chemistry,[2] we present here the divergence of the Rh(II)-catalysed reactions of 1-sulfonyl-1,2,3-triazoles with α-allenols and α-allenones.



References:

[1] a) Chuprakov, S.; Hwang, F. W.; Gevorgyan, V. Angew. *Chem. Int. Ed*. **2007**, *46*, 4757. b) Horneff, T.; Chuprakov, S.; Chernyak, N.; Gevorgyan, V.; Fokin, V. V. *J. Am. Chem. Soc*. **2008**, *130*, 14972. (c) Chuprakov, S.; Kwok, S.W.; Zhang, L.; Lercher, L.; Fokin, V. V. *J. Am. Chem. Soc*. **2009**, *131*, 18034. d) Zibinsky, M.; Fokin, V. V. *Angew. Chem. Int. Ed*. **2013**, *52*, 1507. e) Miura, T.; Tanaka, T.; Biyajima, T.; Yada, A.; Murakami, M. *Angew. Chem. Int. Ed*. **2013**, *52*, 3883. f) Chuprakov, S.; Kwok, S. W.; Fokin, V. V. *J. Am. Chem. Soc*. **2013**, *135*, 4652. g) Parr, B. T.; Green, S. A.; Davies, H. M. *J. Am. Chem. Soc*. **2013**, *135*, 4716. h) Liu, R.; Zhang, M.; Winston-McPherson, G.; Tang, W. *Chem. Commun*. **2013**, *49*, 4376.

[2] a) Progress in Allene Chemistry (issue 9, themed collection); Alcaide, B.; Almendros, P., Eds. *Chem. Soc. Rev*. **2014**, *43*, 2879. b) Alcaide, B.; Almendros, P. *Adv. Synth. Catal*. **2011**, *353*, 2561. c) Alcaide, B.; Almendros, P.; Cembellin, S.; Fernandez, I.; Martinez del Campo, T., *Chem. Commun*. **2016**, 52, 10265. d) Alcaide, B.; Almendros, P.; Martín-Montero, R.; Ruiz, M. P. *Adv. Synth. Catal,* **2016**, *358*, 1469.

Conformational restricted amino acids as inducers of secondary peptide structure

I. Romero-Muñiz[a], M. Martín-Martínez

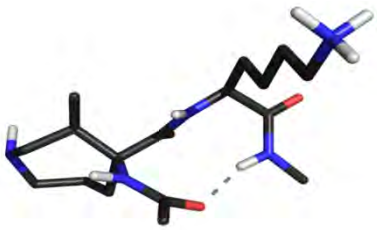
Instituto de Química Médica (IQM-CSIC), Juan de la Cierva 2, 28006 Madrid, Spain
[a]e-mail: ignromer@ucm.es

***Keywords**: foldamers, protein-protein interaction, peptidomimetics.*

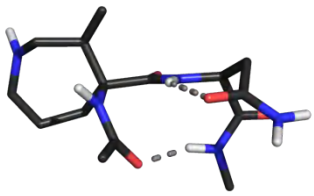
Protein-protein interactions (PPIs) have important roles in many biological and pathological processes. Despite their interest, the development of modulators of these interactions is quite challenging due to their complexity. An approximation to search for these modulations is the design of synthetic mimetics and inducers[1].

Secondary structures such as reverse turns are frequently located at the surface of proteins and are involved in PPIs. Among these motifs, β-turns stand out, being the most common non-repetitive secondary structure in proteins. α,α-Disubstituted amino acids have proved to be adequate inducers of reverse turns and helical structure. In our group, it has been described an α,α-disubstituted azepane derivative (3-aminoazepane-3-carboxylate) with capacity to induce a 3_{10} helix in alanine based peptides[2]. In the present project we analyse the capability of this restricted amino acid to induce reverse turn in peptides with proteinogenic amino acids. Molecular dynamics studies showed that the model tetrapeptide that incorporated this inducer preferentially adopt β-turn conformations. To ascertain experimentally the capacity of the azepane residue (Aze) to stabilize β-turn structures a series of peptide models have been selected for synthesis and subsequent NMR studies.

Ac-Aze-Phe-NHMe



Ac-Aze-Lys-NHMe



Ac-Aze-Asn-NHMe

[1] Nevola, L.; Giralt, E. *Chem. Commun.* **2015**, *51* (16), 3302–3315.
[2] Núñez-Villanueva, D.; Bonache, M. A.; Infantes, L.; Garcia-Lopez, M. T.; Martin-Martinez, M.; Gonzalez-Muniz, R. *J. Org. Chem.* **2011**, *76 (16), 6592–6603.*

Supresión selectiva de señales en RMN mediante cobre como agente PSR (Paramagnetic Spin Relaxation)

L. Socias, J. Correa, R. Riguera, E. Fernandez-Megia*.

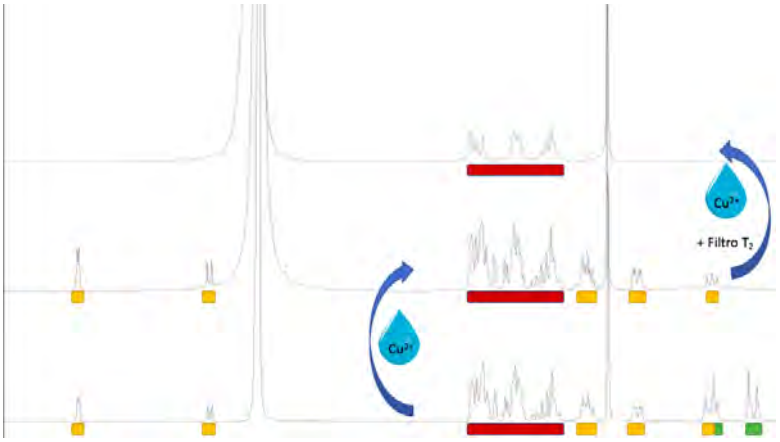
Centro Singular de Investigación en Química Biológica y Materiales Moleculares, Universidad de Santiago de Compostela, 15782 Santiago de Compostela, España
e-mail: sociaspintoll@gmail.com

***Keywords**: RMN, PSR, supresion*

La determinación de muestras farmacéuticas, fluidos biológicos o extractos de productos naturales ha precisado siempre de pasos previos de separación y purificación de sus componentes antes de poder llevar a cabo el análisis. Los avances en espectrometría de resonancia magnética nuclear (RMN) ha permitido poder realizar dicho análisis sin la necesidad de esos pasos previos[1].

Existen diversos métodos para la simplificación de espectros como los filtros de difusión o relajación, que dependen de los tiempos y velocidades de relajación de los diferentes compuestos de la mezcla. Los agentes PSR son capaces de suprimir señales cuando existen compuestos de peso molecular similar[2] y los filtros mencionados no son capaces.

Esta capacidad de los agentes paramagnéticos se debe al poder de complejación con los compuestos presentes, provocando una disminución del tiempo de relajación transversal (T_2) y consecuentemente el ensanchamiento de su señal[3].



En este trabajo se muestran los resultados obtenidos del uso del cobre como filtro PSR aplicado sobre diversas muestras comerciales que contienen mezclas de moléculas de bajo peso molecular.

Referencias:

1. Novoa-Carballal, R.; Fernandez-Megia, E.; Jimenez, C.; Riguera, R. Nat. Prod. Rep. **2011**, 28, 78.

2. Fernandez-Megia, R.; Correa, J.; Novoa-Carballal, R.; Riguera, R. J. Am. Chem. Soc. **2007**, 129, 15164-15173.

3. Correa, J.; Pinto, F. L.; Riguera, R.; Fernandez-Megia, E. Anal. Chem. **2015**, 87, 760- 767.

New synthetic strategies based on bioactive heterocycles and unsaturated systems

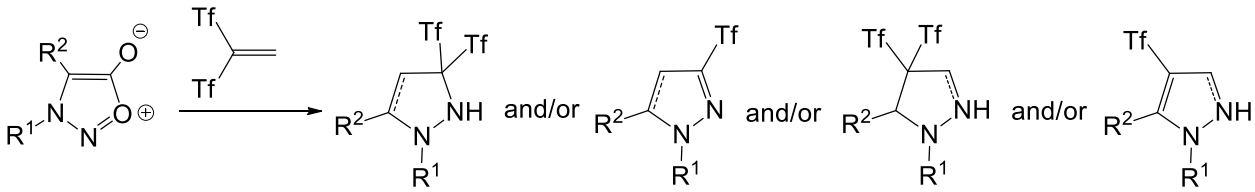
M. Toledano Pinedo[1], B. Alcaide[1], P. Almendros[2], C. Aragoncillo[1] and M. P. Ruiz[1]

[1]*Grupo de Lactamas y Heterociclos Bioactivos, Departamento de Química Orgánica I, Unidad Asociada al CSIC, Facultad de Química, Universidad Complutense de Madrid, 28040-Madrid, Spain.* [2]*Instituto de Química Orgánica General, IQOG-CSIC, Juan de la Cierva 3, 28006-Madrid, Spain.*

e-mail: mireiato@ucm.es

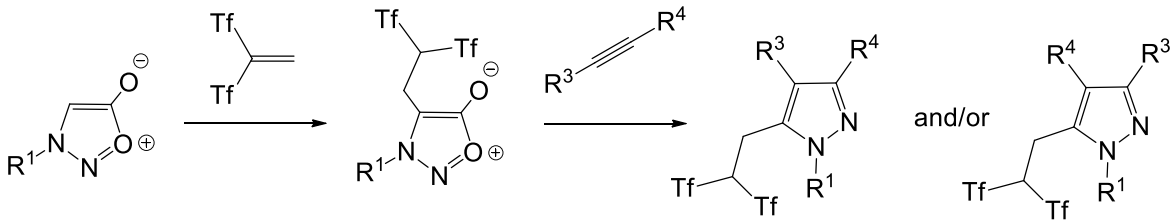
***Keywords**: Sydnone, dipole, cycloaddition.*

Sydnones are 1,3-dipolar compounds used in cycloaddition reactions with several dipolarophiles to produce important heterocyclic products.[1] In this work, the reactivity of different sydnones in presence of a 1,2-dipole generated *in situ* from a zwitterion of Koshar,[2] has been studied affording different structures depending on the sustitution at the position 4 of the sydnone. In particular, we are interested in the regioselectivity of the cycloaddition reaction to give dihidropyrazoles or pyrazoles (Scheme 1).



Scheme 1

In addition, triflone-sydnones were reacted with different alkynes giving rise to new pyrazoles by cycloaddition [3 + 2] (Scheme 2).



Scheme 2

[1] Browne, D. L.; Harrity, J. P.A. *Tetrahedron* **2010**, *66*, 553.

[2] a) Alcaide, B.; Almendros, P.; Fernández, I.; Lázaro-Milla, C. *Chem. Comm.* **2015**, *51*, 3395. b) Alcaide, B.; Almendros, P.; Lázaro-Milla, C. *Chem. Comm.* **2015**, *51*, 6992. c) Alcaide, B.; Almendros, P.; Lázaro-Milla, C. *Chem. Eur. J.* **2016**, *22*, 8998.

SYNTHESIS OF DIMER COMPOUNDS DERIVED FROM HOECHST AND MANNOSE THROUGH CuAAC REACTION

A. Villacampa[a], M. C. de la Torre[a], M. A. Sierra[b]

[a] *Instituto de Química Orgánica General, IQOG, CSIC, Juan de la Cierva 3, 28006-Madrid*
[b] *Grupo de Química Bioorganometálica, Departamento de Química Orgánica I, Facultad de Ciencias Químicas, Universidad Complutense de Madrid, 28040-Madrid*
alejavil@ucm.es

Keywords: *Click Chemistry, DNA Recognition, Carbohydrates*

It has been confirmed that a derivative from Hoechst-Mannose interacts with the DNA minor groove with an affinity constant greater than 10^7 M^{-1}.[1] Based on this results, in this project we propose the synthesis of a series of dimer compounds derived from Hoechst and Mannose. To that purpose we will make react diferent alkynes with 6-azidomonosaccharides using the Copper catalyzed Azide-Alkyne Cycloaddition.[2] Once the corresponding triazoles have been obtained the functionalisation with Hoechst will be sought. In addition, a study will be carried out concerning the possible hydrogen bond formation.

[1] Unpublished results from Diego García-Puentes Doctoral Thesis.
[2] (a) Kolb, C. H.; Finn, M. G.: Sharpless, K. B.; *Angew. Chem. Int. Ed.* **2001**, *40*, 2004-2021 (b) Meldal, M.; Tornoe, C. W.; *Chem. Rev.* **2008**, *108*, 2952-3015.

Synthesis and Reactivity of Triazolyl Sulfoximines

Saúl Alberca Manzano,[a] Roberto Fernández de la Pradilla,[b] Alma Viso,[b] Miguel A. Sierra,[a] María C. de la Torre.[b]

[a] *Departamento de Química Orgánica I, Universidad Complutense de Madrid*
[b] *Instituto de Química Orgánica General (IQOG), CSIC, Juan de la Cierva 3, 28006-Madrid.*
salberca@ucm.es

***Keywords**: sulfoximine; 1,2,3-triazol-5-ylidene; mesoionic carbenes (MICs).*

Sulfoximines are interesting functional groups which have a nitrogen atom attached to a chiral sulfur, so there are many applications in the literature as ligands in asymmetric catalysis or as chiral auxiliaries; in addition, they also play a role in the field of bioactive compounds.[1]

Sulfoximines with a free NH are accessible from sulfoxides by transfer of electrophilic NH,[2] and they are known to act as nucleophiles in alkylation, acylation or sulfonylation reactions, and to participate in a variety of metal-catalyzed coupling processes.

The objective of this work is to explore the transformation of tryazolyl sulfoxides reported by our group,[3] into the unreported NH sulfoximines and to examine the subsequent functionalizations by alkylation, acylation, etc, to fine-tune the electronic properties of the sulfoximinoyl moiety. Finally, the preparation of triazolium salts and mesoionic carbene complexes (MIC) will be addressed.

References:

[1] (a) Frings, M.; Thomé, I.; Schiffers, I.; Pan, F.; Bolm, C. *Chem. Eur. J*. **2014**, *20*, 1700. (b) Reggelin, M.; Weinberger, H.; Gerlach, M.; Welcker, R. *J. Am. Chem. Soc* **1996**, *118*, 4777. (c) Lücking, U. *Angew. Chem. Int. Ed.* **2013**, *52*, 9408.

[2] Zenzola, M.; Doran, R.; Degennaro, L.; Luisi, R.; Bull, J. A. *Angew. Chem. Int. Ed*. **2016**, *55*, 7207.

[3] Frutos, M.; Avello, M. G.; Viso, A.; Fernández de la Pradilla, R.; de la Torre, M. C.; Sierra, M. A.; Gornitzka, H.; Hemmert, C. *Org. Lett*. **2016**, *18*, 3573.

Synthesis of organic ligands for the controlled self-assembly of gold nanorods

José J Garrido González[§], J. Osío Barcina[§], A. Guerrero-Martínez[‡], G. González-Rubio[‡]

[§]*Dpto. de Química Orgánica I, Universidad Complutense de Madrid, Avda. Complutense s/n, 28040 Madrid, Spain*

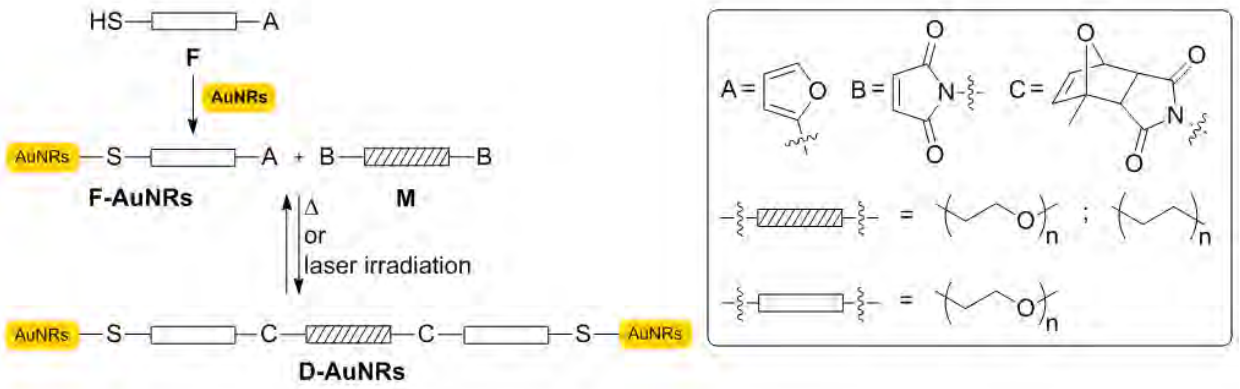
[‡]*Dpto. de Química Física I, Universidad Complutense de Madrid, Avda. Complutense s/n, 28040 Madrid, Spain*

e-mail: jose2garrido@gmail.com

Keywords: *Gold Nanoparticles, Hot Spot, Diels Alder*

Metallic nanoparticles, and among them gold nanoparticles (AuNPs), are structures in the nanometric scale with optical and electronic properties which differ from those belonging to macroscopic and atomic systems. Within these properties, localized surface plasmon resonance[1] (LSPR) derived from the interaction between conduction electrons located on the nanoparticles and an electromagnetic field could generate an increase of temperature (known as hot spot) and a magnetic field located at the AuNPs which are highly dependent on the distance. Specifically, in cylindrical type AuNPs (known as gold nanorods, AuNRs) these hot spots are situated at the end of the nanoparticle.

These properties can be usefully tuned if different parameters like shape, size or distance between AuNPs are modified. There are two main routes for the rational synthesis of gold nanoparticles: the first one uses laser pulses,[1] and the second one is based on the synthesis of thiolated organic ligands[2] used for the stabilization and assembly of these AuNRs. In this work we suggest the use of Diels Alder adducts based on maleimide-furan moieties and the introduction of several poly-ethyleneglycol spacer groups to self-assemble AuNRs, according to the methodology described in scheme 1.



Scheme 1. *Methodology for the assembly of AuNRs*

[1] González-Rubio, G.; Guerrero-Martínez, A.; Liz-Marzán, L.M. *Acc. Chem. Res.* **2016**, *49*, 678.

[2] Coelho, J.P.; González-Rubio, G.; Delices, A.; Osío Barcina, J.; Salgado, C.; Ávila, D.; Peña-Rodríguez, O.; Tardajos, G.; Guerrero-Martínez, A. *Angew. Chem. Int. Ed.* **2014**, *53*, 12751.

Isatin-like Leucine Rich Repeat Kinase 2 (LRRK2) Inhibitors for Parkinson´s disease

A. López García, J. Zaldívar, D.I. Pérez, A. Martínez

Centro de Investigaciones Biológicas, (CSIC), Ramiro de Maeztu,9 ,28040, Madrid, Spain
alopezgarcia18@gmail.com

***Keywords**: LRRK2, isatin, Parkinson´s disease, PARK8*

Parkinson's disease is the second most progressive neurodegenerative disorder affecting older worldwide adults and is predicted to increase as fast as the population grows[1]. Nowadays there is no cure for PD, therefore, it is very important and necessary the pursuit and the development of new drugs able to act as disease-modifying treatments.

One of the most common genetic causes of Parkinson´s disease is mutations in the gen *PARK8/LRRK2* [2]. Inhibition of LRRK2 activity has many neuroprotective benefits and it will provides a means of addressing the underlying biochemical cause of PD for the very first time.

Following a *BIOs* (biology oriented synthesis) approach, a family of *isatin* derivatives were previously described in our work as potent LRRK2 inhibitors able to cross the blood brain barrier [3] . In order to improve the biological activity and physicochemical properties of these compounds, we here expose the synthesis and the biological evaluation of new derivatives, which present different substituents into the *isatin* core.

References:
[1] Beitz. J. M; *Frontiers in Bioscience*, **2014,** *S6*, 65-74
[2] Atashrazm, F; Dzamko, N; *Clinical Pharmologycal: Advances and Applications*, **2016**, *8*, 177-189.
[3] Irene García Salado ; *Doctoral Thesis* ; Univ.Comp. de Madrid, **2014**

Hacia la síntesis de ferrocenil- y ferroceno-quinonas con quiralidad planar y estudio de sus propiedades dador-aceptor

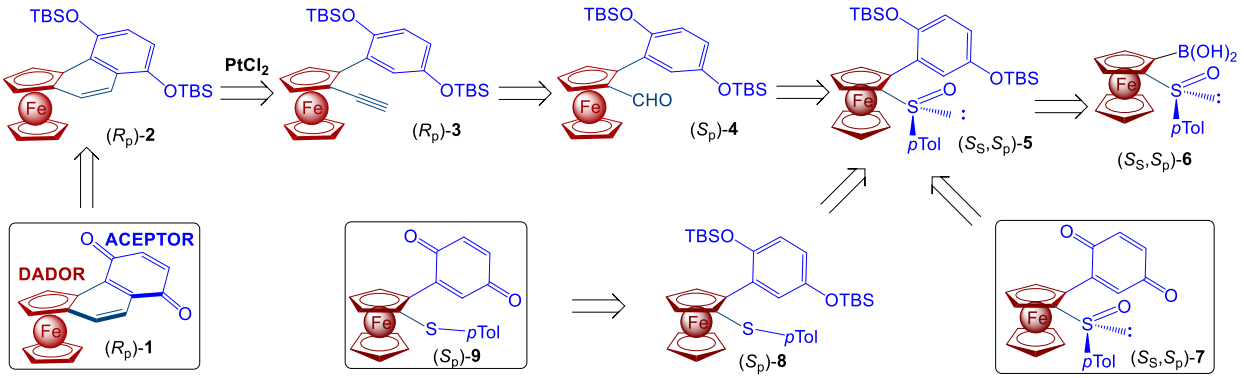
Miguel Alonso de la Peña, Lorena Muñoz, M. Carmen Carreño, Antonio Urbano*

Departamento de Química Orgánica, Universidad Autónoma de Madrid
miguel.alonsod@estudiante.uam.es

***Palabras clave**: ferrocenos, quiralidad planar, quinonas*

En este trabajo, se describen los esfuerzos sintéticos hacia una ferroceno-quinona aromática *orto*-condensada tricíclica con quiralidad planar (R_p)-**1** con el fin de estudiar sus propiedades dador-aceptor. La etapa clave para construir el esqueleto tricíclico, desarrollada previamente en el grupo de trabajo,[1] es la cicloisomerización catalizada por Pt(II)[2] de un alquinil aril ferroceno como (R_p)-**3**.[3] Este derivado se puede obtener después de dos etapas a partir del sufinil ferroceno (S_S,S_p)-**5,** que posee una 1,4-hidroquinona protegida como –OTBS, y que a su vez se obtiene tras un acoplamiento de Suzuki con el ácido borónico con quiralidad planar (S_S,S_p)-**6**.

Aprovechando la preparación del sufinil ferroceno aromático (S_S,S_p)-**5**, se pretende llevar también a cabo la síntesis de la sulfinil ferrocenil quinona con quiralidad planar (S_S,S_p)-**7**, así como la de la sulfenil ferrocenil quinona con quiralidad planar (S_p)-**9**, previa reducción del grupo sulfinilo de (S_S,S_p)-**5** en el correspondiente sufenil ferroceno aromático (S_p)-**8**, para estudiar también sus propiedades dador-aceptor. Los estudios de estas propiedades se realizarán mediante medidas de dicroísmo circular.



Referencias:

[1] a) H. Rodríguez, Trabajo de Fin de Grado, Mayo **2014**. b) A. M. del Hoyo, Tesis Doctoral, Diciembre **2014**. c) R. Barato, Trabajo de Fin de Grado, Mayo **2015**. d) A. Martínez-Carrión, Trabajo Fin de Máster, Julio **2015**. e) A. Kuhne, Trabajo Fin de Máster, Julio **2016**.

[2] V. Mamane, P. Hannen, A. Fürstner, *Chem. Eur. J.* **2004**, *10*, 4556.

[3] A. Urbano, G. Hernández-Torres, A. M. del Hoyo, A. Martínez-Carrión, M. C. Carreño, *Chem. Commun.* **2016**, 6419.

DENDRITIC MICELLES AS DRUG CARRIERS FOR THE TREATMENT OF ALZHEIMER DISEASE

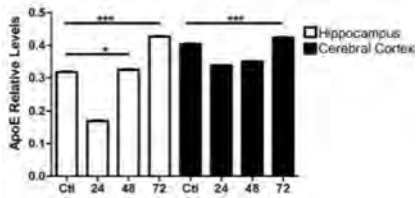
R. López-Blanco,[a] J. Correa,[a] M. Fernández-Villamarín,[a] M. E. Navas,[b] R. Riguera,[a] M. A. Bruno,[b] and E. Fernández-Megía*,[a]

[a] *Centro Singular de Investigación en Química Biológica y Materiales Moleculares (CiQUS), Universidad de Santiago de Compostela, C/ Jenaro de la Fuente s/n, 15782, Santiago de Compostela.* [b] *Laboratorio de Neurociencias-CONICET, Facultad de Ciencias Médicas, Universidad Católica de Cuyo, San Juan, Argentina.*
roi.lopez.blanco@gmail.com

***Keywords**: dendritic micelles, drug delivery, Alzheimer*

Alzheimer is a neurodegenerative and incurable disease in which neuronal degeneration is caused by the abnormal cumulus of β-amyloid (Aβ) peptides on the surface of neurons, leading to senile plaques. While brain's clearance mechanisms, including apolipoprotein E (ApoE), are insufficient to reduce these peptide levels,[1] available drugs are not optimal for the treatment and complex to deliver. In this scenario, the search for new drugs is underway.

DMHCA is a steroid that has demonstrated activity as a hepatic X receptor agonist (LXR).[2] Activation of these receptors results in a higher production of ApoE and therefore a greater and efficient elimination of the Aβ peptides. Insolubility in water is the major limitation of this compound. In this work, we propose the synthesis of block copolymers based on PEG and a 1st generation GATG (gallic acid-triethylene glycol) dendron[3] functionalized with DMHCA, which is able to solubilize the drug via micelle formation. Preliminary studies with these DMHCA's dendritic micelles had demonstrated biological activity, increasing ApoE levels at hippocampus, cerebral cortex and liver.



References:

[1] (a) Saraceno, C.; Musardo, S.; Marcello, E.; Pelucchi, S.; Di Luca, M. *Front. Pharmacol.* **2013**, *4*, 1. (b) Jiang, Q.; Lee, C. Y. L.; Mandrekar, S.; Wilkinson, B.; Cramer, P.; Zelcer, N.; Mann, K.; Lamb, B.; Willson, T. M.; Collins, J. L.; Richardson, J. C.; Smith, J. D.; Comery, T. A.; Riddell, D.; Holtzman, D. M.; Tontonoz, P.; Landreth, G. E. *Neuron.* **2008**, *58*, 681.

[2] Boehm-Cagan, A.; Michaelson, D. M. J. *Neurosci.* **2014**, *34*, 7293.

[3] (a) Fernández-Villamarín, M.; Sousa-Herves, A.; Correa, J.; Munoz, E. M.; Taboada, P.; Riguera, R.; Fernández-Megía, E. *ChemNanoMat* **2016**, *2*, 437. (b) Sousa-Herves, A.; Novoa-Carballal, R.; Riguera, R.; Fernández-Megía, E. *AAPS J.* **2014**, *16*, 948.

Reacciones de Fotoalquilación Asimétrica Intramolecular de Aldehídos

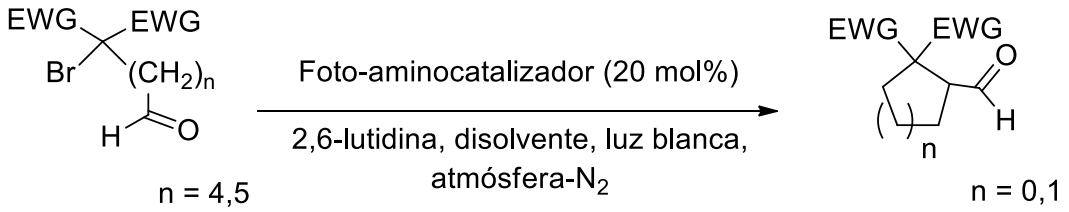
D. Álvarez Fernández, T. Fischer, T. Rigotti, A. Casado Sánchez, J. Alemán.

Departamento de Química Orgánica, Facultad de Ciencias, Universidad Autónoma de Madrid
e-mail: delia.alvarezf@estudiante.uam.es

***Palabras clave**: fotocatálisis, organocatálisis, aldehídos.*

La fotocatálisis y la organocatálisis han aparecido en la última década como nuevas áreas muy eficaces para la activación de moléculas. La combinación de ambas da lugar a nuevos métodos de síntesis de moléculas y aporta grandes ventajas para llevar a cabo una química con menos impacto medioambiental: los organocatalizadores son menos tóxicos y más económicos, los tiempos de reacción en general son menores, la fotocatálisis se realiza con luz visible y los catalizadores se pueden recuperar. Por otro lado, la búsqueda de nuevas formas de α-alquilación asimétrica de aldehídos distintas a las tradicionales es uno de los objetivos de la fotocatálisis asimétrica. Por ello, la combinación de la fotocatálisis con la organocatálisis asimétrica promueve nuevos métodos para la síntesis de moléculas enantioméricamente puras.

En la presente comunicación se presenta una reacción que hasta el momento no ha sido descrita en la bibliografía: la reacción intramolecular fotocatalítica de aldehídos. A partir de aldehídos **1** se han realizado distintas reacciones, modificando las condiciones como son el fotocatalizador y el aminocatalizador, disolventes, temperatura o concentración para conseguir altos rendimientos y excesos enantioméricos.



1 **2**

Reacción intramolecular fotocatalítica de aldehídos. (EWG = grupo atractor de electrones).

Referencias:
[1] Nicewicz, D.A.; MacMillan D.W.C. *Science*, **2008**, 322, 5898.
[2] Meggers, E. *Chem. Commun.* **2015**, *51*, 3290.
[3] Prier, C. K.; Rankic, D. A.; MacMillan D.W.C. *Chem. Rev.* **2013**, *113*, 5322.

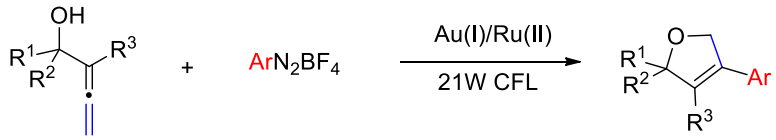
NUEVAS ESTRATEGIAS SINTÉTICAS BASADAS EN ALENOS Y HETEROCICLOS BIOACTIVOS

B. Aparicio[1], B. Alcaide[1], P. Almendros[2], A. Luna[1]

[1]Grupo de Lactamas y Heterociclos Bioactivos, Departamento de Química Orgánica I, Unidad Asociada al CSIC, Facultad de Química, Universidad Complutense de Madrid, 28040-Madrid, España; [2]Instituto de Química Orgánica General, IQOG, CSIC, Juan de la Cierva 3, 28006-Madrid, España.
borjaapa@ucm.es

***Keywords**: allenes, catalysis, photoredox.*

Allenes are a class of compounds with two cumulated carbon-carbon double bonds, which are versatile synthetic intermediates in organic synthesis.[1] They have shown an interesting reactivity and selectivity affording complex structures in a limited number of steps using a wide variety of transition metals.[2] Particularly, the cyclization of allenes bearing nucleophilic centres has been achieved regio- and stereoselectively using gold catalysis.[3] On the other hand, visible light photoredox catalysis emerged as a new and powerful mode to activate small molecules.[4] Surprisingly, the gold-photoredox cocatalyzed tandem oxycyclization/coupling of allenols has not been reported. For this reason, in this work, we describe a tandem sequence allenol oxycyclization/aryl diazonium salt cross-coupling for the controlled direct preparation of substituted tetrahydrofurans under mild conditions.



References:

[1] (a) Allen, A. D.; Tidwell, T. T.; *Chem. Rev.* **2013**, *113*, 7287; (b) Yu, S.; Ma, S. *Angew. Chem. Int. Ed.* **2012**, *51*, 3074; (c) Ma, S. *Chem. Rev.* **2005**, *105*, 2829; (d) Modern Allene Chemistry Krause, N. Hashmi, A. S. K. Eds.; Wiley-VCH, Weinheim, **2004**.
[2] (a) *Progress in Allene Chemistry*; Ed.; Alcaide, B.; Almendros, P. *Chem. Soc. Rev.* **2014**, *43*, issue 9. (b) Alcaide, B.; Almendros, P.; Martinez del Campo, T.; Soriano, E.; Marco-Contelles, J.L. *Top. Curr. Chem.* **2011**, *302*, 183. (c) Alcaide, B.; Almendros, P. *Chem. Rec.* **2011**, *11*, 311.
[3] (a) Alcaide, B.; Almendros, P.; Quirós, M. T.; Matínez del Campo, T.; Soriano, E.; Marco-Contelles, J. L. *Chem. Eur. J.* **2013**, *19*, 14233. (b) Alcaide, B.; Almendros, P.; Cembellín, S.; Martínez del Campo, T.; Fernández, I. *Chem. Commun.* **2013**, *49*, 1282; (c) Alcaide, B.; Almendros, P.; Alonso, J. M.; Fernández, I. *Chem. Commun.* **2012**, *48*, 6604.
[4] (a) Cambié, D., Noël, T. Chem. Rev. 2016, 116, 10276; (b) Hoffmann, N. Synthesis 2016, 48, 1782; (c) MacMillan, D. W. C., Prier, C. K. Chem. Rev. 2013, 113, 5322.

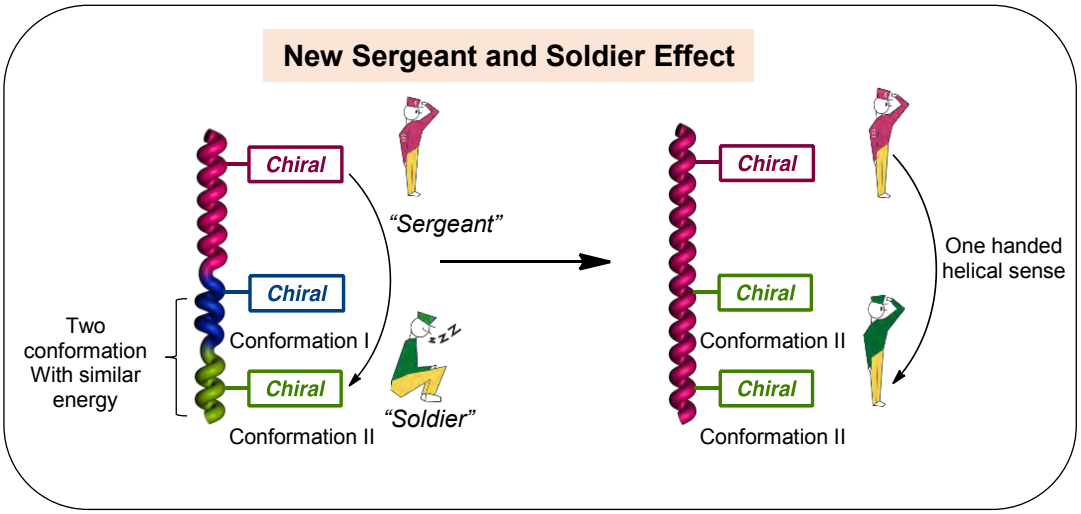
Chiral-to-chiral communication in helical polymers

N. Barbón, E. Quiñoa, F. Freire

CIQUS- Campus Vida- Universidad de Santiago de Compostela
e-mail: natalia.barbon@rai.usc.es

***Keywords**: (Seargent-Soldier effect, helical polymers, polyphenylacetylenes)*

The role of the absolute configuration, conformation, and helical scaffold that promote the parent monomers in the corresponding homopolymers[1] are taken into account to explain their consequences on the helix enhacement of the copolymer. Thus, we found from different 2 copolymer series that a chiral to chiral communication mechanism just happen between monomers that have different conformational flexibility and that give rise to polymers with resembled structures. This phenomenom can be denoted as chiral Sergeant and chiral soldier effect[2,3,4], and can be used to induce or amplify a helical sense in poorly folded chiral polymer. In our system the chiral Soldier includes either (*R*)- or (*S*)-2-methoxy-2-phenylacetamide substituent linked to the main backbone in para position and is characterized by its conformational flexibility[5]. The chiral Sergeant contains a similar group linked to the backbone in meta position and is selected on the basis of its restricted conformation. Incorporation of a very small amount of the Sergeant to a chain composed just by the Soldier transforms the originally axially racemic chain into a helix with strong sense preference (either *M* or *P*) that is determined by the absolute configuration of the Soldier. The high efficiency of this approach allows a new way to convert helical polymers with low or null sense preference into fully oriented ones, without having to resort to any kind of external stimuli.



References:

[1]. R. Rodríguez, E. Quiñoá, R. Riguera, F. Freire, *J. Am. Chem. Soc*. **2016**, *138*, 9620
[2]. M. M. Green, M. P. Reidy, R. J. Johnson, G. Darling, D. J. Oleary, G. Willson. *J. Am. Chem. Soc*. **1989**, *111*, 6452.
[3]. J. Bergueiro, F. Freire, E. P. Wendler, J. M. Seco, E. Quiñoá, R. Riguera. *Chem. Sci*. **2014**, *5*, 2170
[4]. S. Arias; J. Bergueiro; F. Freire; E. Quiñoá; R. Riguera, *Small*, **2016**, *12*, 238.
[5]. F. Freire, J. M. Seco, E. Quiñoá, R. Riguera, *Angew. Chem., Int. Ed*. **2011**, *50*, 11692.

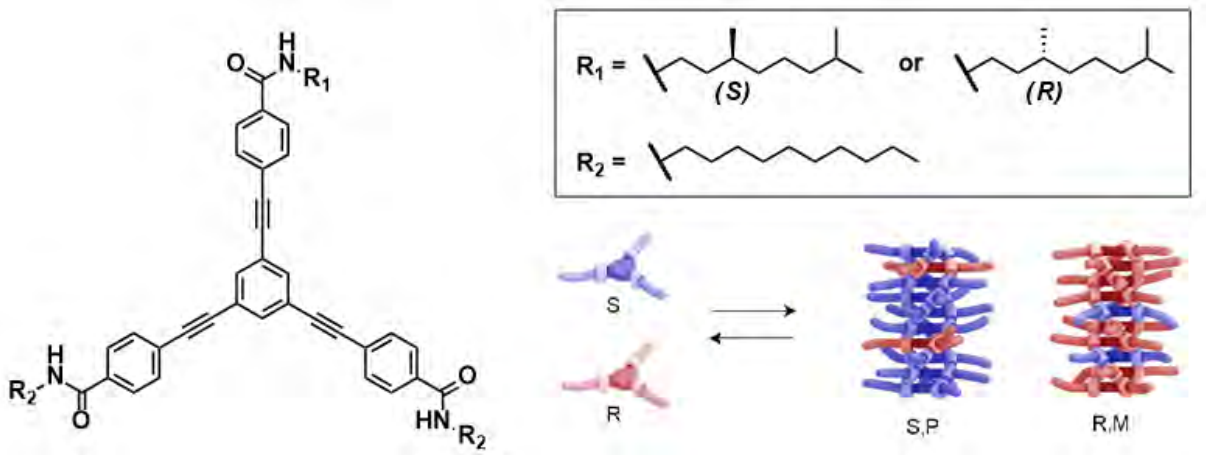
SYNTHESIS OF ASYMMETRIC TRICARBOXAMIDES ENDOWED WITH POINT CHIRALITY. TRANSFERENCE AND AMPLIFICATION OF CHIRALITY

M. Buendia, J. S. Valera, L. Sánchez

Grupo de Moléculas Anfifílicas y Polímeros Supramoleculares
Universidad Complutense de Madrid (UCM), Departamento de Química Orgánica I
manubuen@ucm.es, lusamar@quim.ucm.es

***Keywords**: supramolecular polymers, transfer of chirality, amplification of chirality*

Oligo(phenylene ethynylene) (OPE) derivatives are compounds known for their tendency to form supramolecular aggregates in solution.[1] Herein, we present the synthesis of two OPEs endowed with three amide functional groups and only one stereogenic center of absolute configuration (R or S) at the peripheral side chains. The stereogenic center bias the chirality of the formed helical structure, leading to a preferred handedness. The capability of these compounds to self-assemble has been demonstrated by FTIR, ^{1}H-NMR and circular dichroism (CD) experiments which led to the elucidation of a cooperative supramolecular polymerization mechanism. In addition, the ability of the reported tricarboxamides to transfer and to amplify chirality has been investigated. A clear CD response is observed upon the self-asssembly of the reported tricarboxamides, diagnostic of an efficient transfer of chirality. However, majority rules experiments demonstrate that only a weak amplification of chirality takes place.[2] The results presented in this study lead to a better understanding of the parameters governing the supramolecular polymerization process and contribute to shed light on the origin of homochirality in nature.



[1] a *J. Am. Chem. Soc.*, **2012**, *134*, 734; b) García, F.; Korevaar, P. A.; Verlee, A.; Meijer, E. W.; Palmans, A. R. A.; Sánchez, L. *Chem. Comm.*, **2013**, *49*, 8674.
[2] Smulders, M. M. J.; Filot, I. A. W.; Leenders, J. M. A.; Schoot, P.; Palmans, A. R. A.; Schenning, A. P. H. J.; Meijer, E. W. *J. Am. Chem. Soc.*, **2010**, *132*, 611.

Synthesis of Chiral Iridium-Fullerene Complexes

Gorka Calvo Martín, Salvatore Filippone

Universidad Complutense de Madrid
Gorkacal@ucm.es

***Keywords**: Fullerenes, Chirality, Catalysis*

Fullerenes have attracted wide interest in chemistry because of their singular round shape and physicochemical properties.[1, 2] The control of chirality in these carbon allotropes is a key point for their application in material science or medicinal chemistry among others. In this project we describe the synthesis of iridium-fullerene hybrids with a complete control of four stereocenters; being one of them an iridium atom.[3, 4] To this aim, different substituted pyrrolidines were synthesized and reacted with iridium-Cp* dimers, leading to the stereoselective formation of a sole optically active iridum-fullerene complex (figure 1). These fullerene-metal hybrids will be tested, in the future, for their potential as a catalysts for a variety of (stereo)chemical reactions, such a hydrogen transfer reactions.[5]

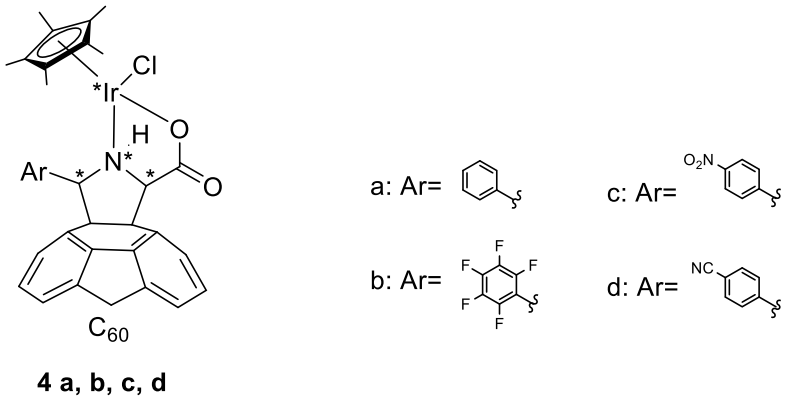


Figure 1: Chiral iridium-fullerene hybrids with direfent aromatics subtituents at the pyrrolidine

References:

[1] Kroto, H. W.; Heath, J. R.; O´Brien, S. C.; Curl, R. F., "C_{60}: buckminsterfullerene", *Nature* **1985**, *318*, 162-163.
[2] Echegoyen, L.; Dietrich, F.; Echegoyen, L. E., *Fullerenes: Chemistry, Physics and Technology* (Ed. Ruoff R.S.), John Wiley & Sons, Inc., New York, 2000; pp. 1-51.
[3] Maroto, E. E.; Izquierdo, M.; Reboredo, S.; Marco-Martinez, J.; Filippone, S.; Martín, N., "Chiral Fullerenes from Asymmetric Catalysis", *Acc. Chem. Res*. **2014**, *47*, 2660-2670
[4] Marco-Martinez, J.; Vidal, S.; Fernandez, I.; Filippone, S.; Martín, N., "Stereodivergent-at-metal synthesis of [60]Fullerene hybrids", *Angew. Chem. Int. Ed*. **2017**, *56*, 1-5.
[5] Vidal, S.; Marco-Martinez, J.; Filippone, S.; Martín, N., "Fullerenes for catalysis: Metallofullerenes in hydrogen transfer reactions", *Chem. Comm*. **2013**, *00*, 1-3.

SYNTHESIS OF PHOTO- AND ELECTROACTIVE DERIVATES BASED ON CARBON NANODOTS

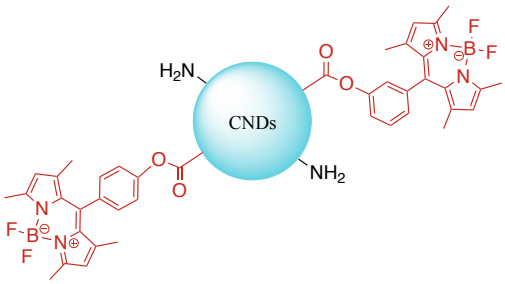
A. Carrión-Rus,[a] A. Ferrer-Ruiz,[a] L. Rodríguez-Pérez,[a] M. A. Herranz,[a] N. Martín[a,b]

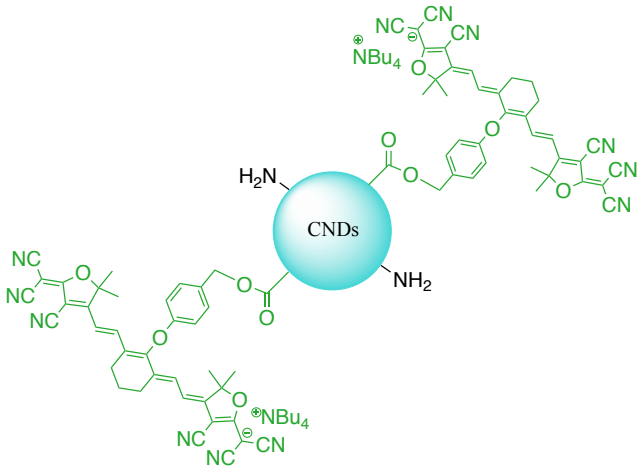
[a] *Departamento de Química Orgánica I, Facultad de Ciencias Químicas, Universidad Complutense, 28040, Madrid, Spain*
[b] *IMDEA-Nanoscience, C/Faraday, 9. Ciudad Universitaria de Cantoblanco, 28049, Madrid, Spain*
e-mail: alcarr02@ucm.es

Keywords: *carbon nanodots, organic dyes, electroactive materials*

Carbon Nanodots (CNDs) are a type of fluorescent nanomaterials based on carbon which have recently attracted great interest due to their outstanding optical properties,[1] their easy synthesis from simple molecular precursors, and their potential application in research areas such as biomedicine, sensors or catalysis.[2]

We have carried out the synthesis of these nanoparticles starting from two straightforward and economically affordable reactants such as citric acid and urea, by following a straightforward heating process in a microwave reactor. After their isolation, these systems have been further functionalized with molecular precursors that are also fluorescent: BODIPY derivatives and an anionic derivative of the cyanines family,[3] with the objective to obtain emissive materials that can act as chromophore antennas that absorb in the whole UV-vis spectrum. For this reason, the CNDs have been linked to the desired organic precursor via esterification reactions. In order to characterize the obtained CNDs and its properties, several techniques have been used, such as Magnetic Nuclear Resonance (NMR), Fourier Transform Infrared spectroscopy (FTIR), UV-vis-NIR spectroscopy, Thermogravimetric Analysis (TGA), X-ray diffraction, Transmission Electron Microscopy (TEM) and Atomic Force Microscopy (AFM). All these results will be presented and discussed in the symposium.





References:

[1] Cayuela, A.; Soriano, M. L.; Carrillo-Carrión, C.; Valcárcel, M. *Chem. Commun.* **2016**, *52*, 1311.
[2] Vázquez-Nakagawa, M.; Rodríguez-Pérez, L.; Herranz, M. A.; Martín, N. *Chem. Commun.* **2016**, *52*, 665.
[3] a) Liu, J-Y.; Yeung, H-S.; Xu, Y.; Li, X.; Dennis, K. P. *Org. Lett.* **2008**, *10*, 5421. b) Roth, A.; Schierl, C.; Ferrer-Ruiz, A.; Minameyer, M.; Rodríguez-Pérez, L.; Villegas, C.; Herranz, M. A.; Martín, N.; Guldi, D. M. *Chem.* **2017**, *In press*.

SUPRAMOLECULAR STRATEGY TO TUBULAR NANOSTRUCTURES SELF-ASSEMBLED FROM DINUCLEOBASE MONOMERS IN AQUEOUS MEDIA

P. B. Chamorro,[1] R. Chamorro,[1] F. Aparicio,[1] D. González-Rodríguez*[1]

[1] *Nanostructured Molecular Systems and Materials* group, Departamento de Química Orgánica, Universidad Autónoma de Madrid, 28049, Madrid, Spain. E-mail: paula.chamorro@estudiante.uam.es

***Keywords**: Self-assembly, nanotubes, nucleobases.*

Tube-forming proteins, such as tubulin or aquaporin are fascinating class of self-assembled functional systems found in nature. Driven by their large variety of functions and their nanometer dimensions, scientists are increasingly being attracted to the challenge of designing related nanoscale assemblies. Our project, inspired by these natural systems, aims at establishing a strategy to prepare tubular nanostructures[1] based on complementary dinucleobase monomers featuring an amphiphilic central block, which can self-assemble in aqueous media by diverse noncovalent interactions. Watson-Crick H-bonding[2] produces macrocyclic tetramers[3-6] with a hydrophobic core, that can stack through hydrophobic forces to yield the desired nanotubes. On the other hand, the hydrophilic chains oriented to the periphery would help to improve water solubility.

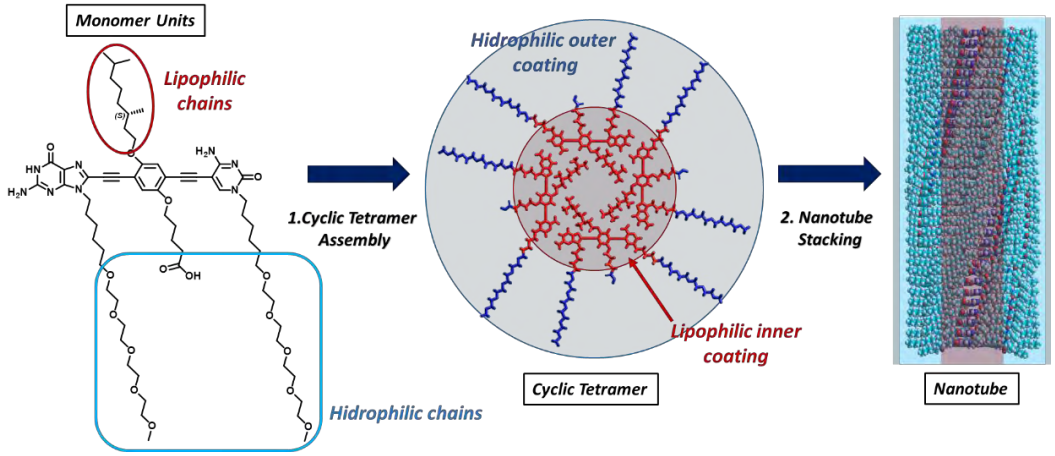


Figure 1. Schematic illustration of the stepwise self-assembly process.

Referencias

[1] J. Couet et al., *Soft Matter* **2006**, *2*, 1005-1014.
[2] M. J. Mayoral, C. Montoro-García, D. González-Rodríguez, in *Comprehensive Supramolecular Chemistry II*, **2016**, http://dx.doi.org/10.1016/B978-0-12-409547-2.12536-3.
[3] C. Montoro-García, J. Camacho-García, A. M. López-Pérez, N. Bilbao, S. Romero-Pérez, M. J. Mayoral, D. González-Rodríguez, *Angew. Chem. Int. Ed.* **2015**, *54*, 6780-6784.
[4] M. J. Mayoral, N. Bilbao, D. González-Rodríguez, *ChemistryOpen*, **2016**, *5*, 10-32.
[5] C. Montoro-García, J. Camacho-García, A. M. López-Pérez, M. J. Mayoral, N. Bilbao, D. González-Rodríguez, *Angew. Chem. Int. Ed.* **2016**, *55*, 223-227.
[6] N. Bilbao, I. Destoop, S. De Feyter, D. González-Rodríguez, *Angew. Chem. Int. Ed.* **2016**, *55*, 659-663.

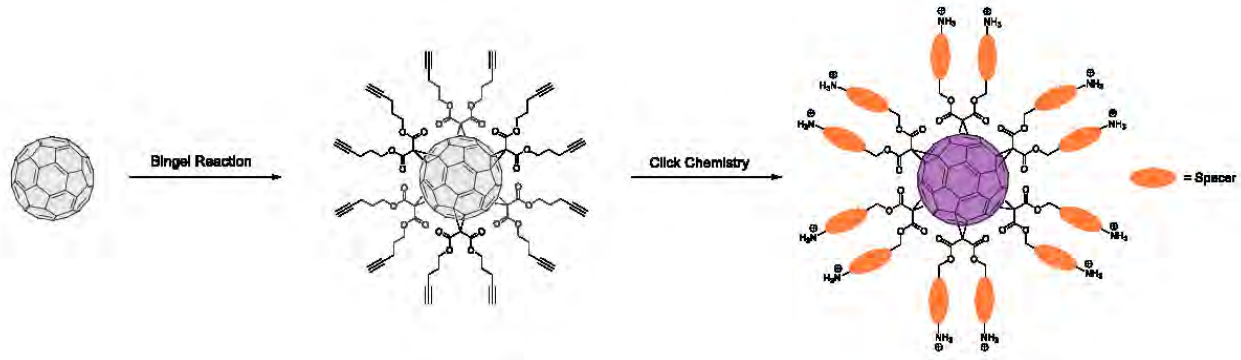
Synthesis of fullerene derivatives capable of being used as non-viral vectors in transfection processes

A. Espiñeira-Gutiérrez, A. Pérez-Sánchez, A. Martín-Domenech, B.M. Illescas, N. Martín

Dpto. Química Orgánica, Facultad de CC. Químicas, Universidad Complutense de Madrid, Madrid, Spain
adriespi@ucm.es

***Keywords**: transfection, fullerene, click chemistry*

Transfection is a process by which external genetic material is introduced into a cell in order that the once assimilated cell expresses the new genetic information. This technique is carried out thanks to the use of transfection vectors that compact genetic material and avoid degradation of said material[1]. In this work, fullerene-C_{60} derivates are synthesized that can be used as transfection vectors; for this it is necessary to functionalize the fullerene molecule properly with protonable amino residues that allow to reach a suitable solubility to physiological pH. Bingel cycloaddition and "click chemistry" reaction have been used in order to achieve this objective[2]. Once synthesized it is intented to evaluate the biological activity of said compounds.



References:
[1] Mintzer, M.A.; Simanek, E.E.; *Chem. Rev.* **2009**, *109*, 59.
[2] Muñoz, A.; Sigwalt, D.; Illescas, B.M.; Luckzowiak, J.; Rodríguez-Pérez, L.; Nierengarten, I.; Holler, M.; Remy, J-S.; Buffet, K.; Vincent, S.P.; Rojo, J.; Delgado, R.; Nierengarten, J-F.; Martín, N.; *Nature Chemistry*, **2016**, *8*, 50-57.

Glycopeptides for protein selective recognition and cellular internalization

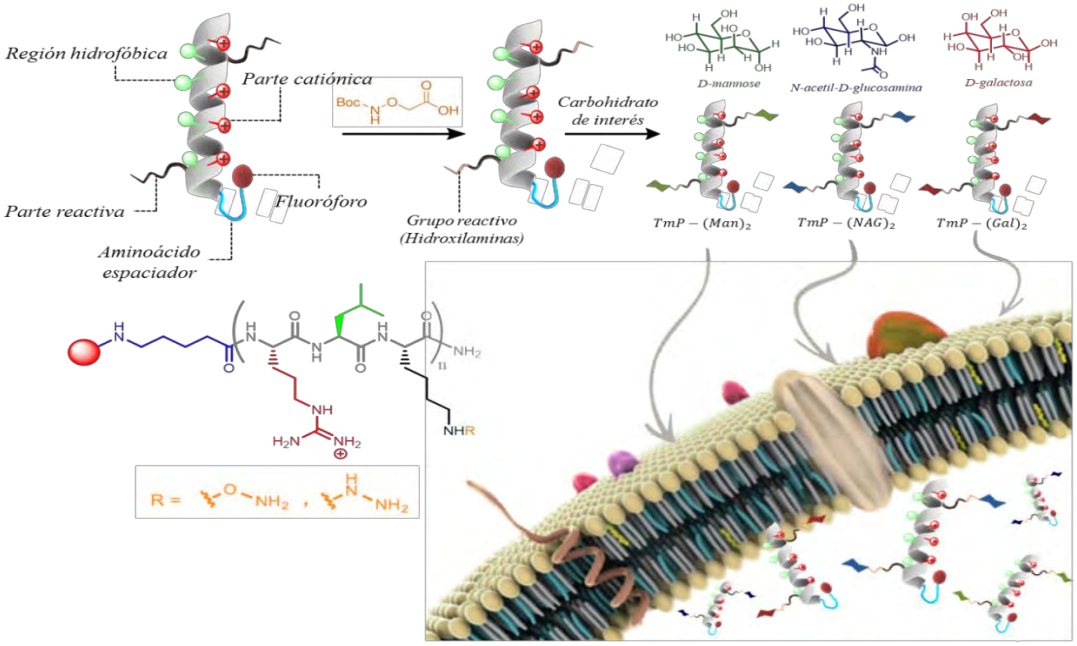
I. Gallego[1], M. Juanes[1], Jose J. Reina[1], J. Granja[1], J. Montenegro[1]

[1]*Centro Singular de Investigación en Química Biolóxica e Materiais Moleculares (CIQUS), Universidade de Santiago de Compostela (USC), 15782 Santiago de Compostela, A Coruña.*

ivan.gallego@rai.usc.es

***Keywords**: Glycochemistry, Cell-penetrating peptides (CPPs), Biological chemistry.*

The overexpression of membrane proteins is a common phenotype of disease and malignant tumours. The cell membrane is essential for the regulation of functions and the exchange of information. However, in many occasions, the lipid bilayer constitutes a barrier for the internalization of bioactive molecules and treatment of diseases. The possibility of controlling the traffic of proteins across the cell membrane represents a unique opportunity to understand and to develop new therapies and diagnose methods. [1]



The first objective of this project is the synthesis of different peptides incorporating cationic and hydrophobic domains to trigger membrane translocation. Additionally, these peptides will be modified with alkoxyamines residues for the anchoring of glycan molecules. Moreover, we would study the selective internalization and the cellular penetration behavior of different glycopeptides by epifluorescence microscopy and flow cytometry. The last objective of this project will be the study of different cellular lines as well as the study with endocytosis inhibitors.

We acknowledge the support from MINECO (CTQ2014-59646-R) and the Xunta de Galicia (ED431G/09 and 2016-AD031), the ERDF, the ERC Starting Grant (DYNAP-677786), the Human Frontier Science Program (RGY0066/2017) and the Foundation Segundo Gil Dávila.

[1] J. A. Zuris, D. B. Thompson, Y. Shu, J. P Guilinger, J. L. Bessen, J. H. Hu, M. L. Maeder, J. K. Joung, Z-Y. Chen, D. R. Liu. *Nat. Biotech.* **2015**, *33*, 73–80.

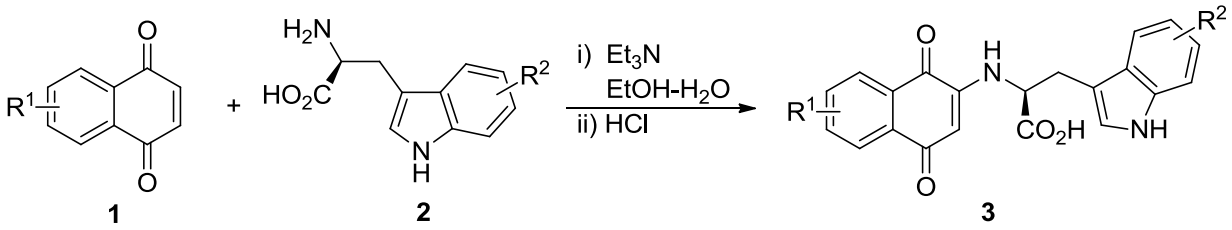
SYNTHESIS OF NEW RADIOTRACERS FOR SENILE PLAQUE DETECTION BY ^{18}F-PET

A. González Molina, S. Roscales, A. G. Csákÿ*

Instituto Pluridisciplinar. Universidad Complutense de Madrid. Paseo de Juan XXII, 1. Madrid, Spain
alvago08@ucm.es, silviarg86@hotmail.com, csaky@ucm.es

***Keywords**: Senile plaques, Alzheimer, radiotracer*

Dementia is a neurodegenerative syndrome characterized by a loss of memory and other cognitive abilities. There are numerous diseases that evolve with dementia, and among them, Alzheimer´s disease is (AD) is the most common cause. There is no direct means of diagnosing this disease. Definite clinical evidence can only be obtained *postmortem* after a histological study of the brain.[1] From a histopathological standpoint, the post-mortem examination of the brains of patients diagnosed with AD presents two main features which are considered biomarkers of the disease: Intraneuronal neurofibrillary tangles (NFTs), composed by paired helicoidal filaments of tau hyperphosphorilated protein (PHF-tau), and extracellular fibrilar deposits of β-amyloid peptide (Aβ), that constitute the so-called senile plaques (SPs). In this work, a series of quinone-amino acid hybrids have been designed to evaluate their affinity for amyloid plaques, in order to design new radiotracers to monitor *in vivo* the evolution of AD by Positron Emission Tomography (PET).[2,3] Among commonly used radionuclides in PET tracer development, ^{18}F is the most used due to its relative long half lifetime (110 min), which permits the accomplishment of the radiosynthesis, and the possibility of acting as a hydrogen bioisoster. The development of these ^{18}F-PET radiotracers may help diagnosis in the early stages of the disease.



***Scheme 1.** Synthesis of quinone – amino acid hybrids as ^{18}F-PET radiotracers for AD*

[1] Oukoloff, K.; Cieslikiewicz-Bouet, M.; Chao, S.; Da Costa Branquinho, E.; Boutellier, C.; Jean, L.; Renard, P.-Y. *Curr. Med. Chem.* **2015**, *22*, 3278. [2] Scherzer-Attali, R.; Convertino, M.; Pellarin, R.; Gazit, E.; Segal, D.; Caflisch, A. *J. Phys. Chem. B* **2013**, *117*, 1780. [3] Katritzky, A. R.; Huang, L.; Sakhuja, R. *Synthesis* **2010**, *12*, 2011.

Síntesis enantioselectiva de ciclobutilboronatos mediante reacciones de carboboración catalizadas por Cu (I)

Víctor García Vázquez, Víctor Martín Heras, Alejandro Parra y Mariola Tortosa*.

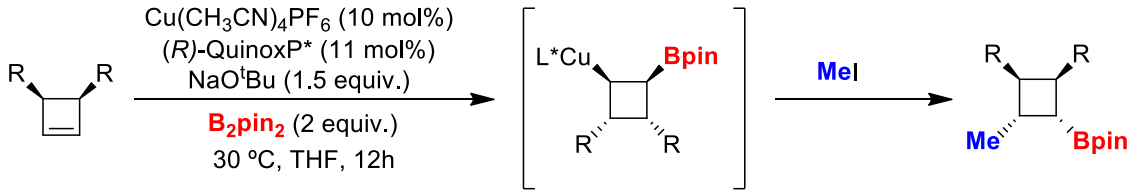
Universidad Autónoma de Madrid
victor.garciav@estudiante.uam.es

***Keywords**: Cyclobutylboronates, copper-catalyzed, carboboration*

Los ciclobutilboronatos enantioméricamente puros son compuestos con un elevado potencial sintético. Por ello, nuestro grupo de investigación se propuso llevar a cabo la desimetrización de anillos de ciclobutenos mediante reacciones de hidroboración catalizadas por Cu(I).[1] Para ampliar la utilidad de esta reacción, en este trabajo se ha explorado la posibilidad de llevar a cabo una carboboración enantioselectiva catalizada por Cu(I) de *meso*-ciclobutenos.

Para sintetizar los materiales de partida se han utilizado tres rutas sintéticas distintas. Una de ellas está basada en la reacción electrocíclica disrotatoria de cierre de anillo de un derivado de cicloheptadieno. Los otros dos métodos son más complejos, y requieren de varias etapas sintéticas, teniendo como etapa clave una cicloadición [2+2] de una cetena con un alqueno o alquino.

Posteriormente, se han optimizado las condiciones de reacción para la carboboración catalizada por Cu(I), y se han utilizado estas condiciones con los materiales de partida sintetizados. De esta manera, se han preparado ciclobutilboronatos enantiomericamente puros con cuatro centros estereogénicos contiguos.



Esquema 1: Carboboración de ciclobutenos catalizada por Cu(I).

[1] Guisán-Ceinos, M.; Parra, A.; Martín-Heras, V.; Tortosa, M. *Angew. Chem. Int. Ed.* **2016**, *55*, 6969.

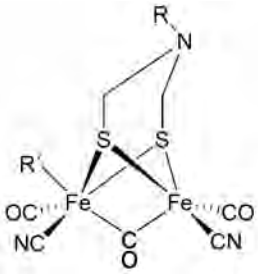
Hydrogenase Mimetics for Hydrogen Production

Diego J. Vicent, Maria Frutos[1,2]; Mar Gomez-Gallego[1,2]; Miguel A. Sierra[1,2]

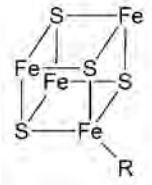
1 Departamento de Química Orgánica I, Facultad de Química, Universidad Complutense, 28040-Madrid, Spain.
2 Centro de Innovación en Química Avanzada (ORFEO-CINQA).
e-mail: djimen01@ucm.es

***Keywords**: Fe-Fe Hidrogenases, metallocene.*

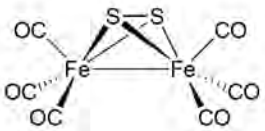
The need to replace fossil fuels as an energy source is one of the major scientific challenges of the 21st century. There are different scientific routes to solve this problem, and one of the most promising is the use of hydrogen as an alternative energy source.
Hydrogenases are metalloenzymes responsible for the hydrogen production of certain anaerobic microorganisms, and their mode of action has excited the interest of various research groups. It is known that the active center of the Fe-Fe hydrogenases is formed by Fe_2S_2 **1** and Fe_4S_4 **2** clusters, and the cluster **3** has structural properties very similar to the Fe_2S_2 complex.[1]
The challenge of this project is to join the cluster covalently to two metallocenes, **4a** and **4b**, in order to obtain two hydrogenase mimetics. On the other hand, the synthesis of another mimetic is sought, in order to attach the cluster unit to a doped metal surface.
In both cases the redox and electronic properties of the compounds synthesized will be evaluated to determine the effect caused by the presence of other metals on the reduction potential of the cluster.



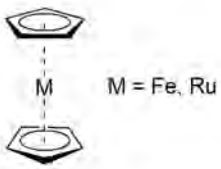
1



2



3



4a/4b

References:

[1] (a) Schilter, D.; Camara, J. M.; Huynh, M. T.; Hammes-Schiffer, S.; Rauchfuss, T. B. *Chem. Rev.* **2016**, *116,* 8693. (b) Li, Y.; Rauchfuss, T. B. *Chem. Rev.* **2016**, *116,* 7043.

Síntesis de un conector molecular con simetría trigonal para la unión de tres cintas de grafeno sobre superficie.

Mariño, F.; Guitián, E.; Pérez, D.; Peña, D.

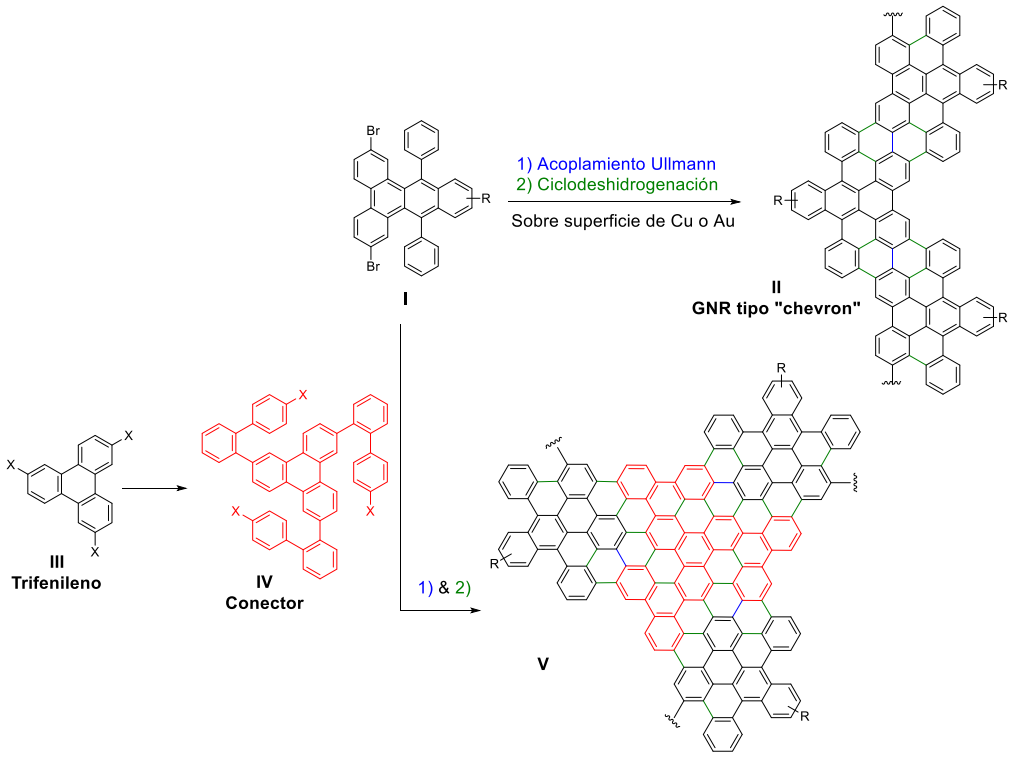
Departamento de Química Orgánica y Centro Singular de Investigación en Química Biológica y Materiales Moleculares (CiQUS), Universidad de Santiago de Compostela, C/ Jenaro de la Fuente s/n, 15782, Santiago de Compostela

fatima.marino@rai.usc.es

***Keywords**: Arinos, trifenileno, cintas de grafeno.*

Las cintas de grafeno (GNRs) han despertado un enorme interés en nanotecnología por su posible aplicación en electrónica molecular, por ejemplo como cables moleculares, donde la conductividad dependería de la forma y anchura de las cintas.[1] Sin embargo, para el desarrollo de esta electrónica molecular basada en GNRs, es imprescindible disponer de conectores que permitan unir varias cintas. En este trabajo avanzamos en el desarrollo de un conector específicamente diseñado para unir tres cintas de grafeno de tipo "chevron" (**II**) como se indica en la figura.[2]

Se prepararon trifenilenos trihalogenados (**III**) con el fin de obtener conectores moleculares con estructura trigonal (**IV**) para la unión de tres GNRs tipo "chevron" (**V**) sobre superficie. Los trifenilenos trihalogenados (**III**) necesarios para la preparación de los conectores (**IV**) se obtuvieron utilizando la química de arinos desarrollada en el grupo de investigación.[3]



[1] Ruffieux, P.; Wang, S.; Yang, B.; Sánchez-Sánchez, C.; Liu, J.; Dienel, T.; Talirz, L.; Shinde, P.; Pignedoli, C. A.; Passerone, D.; Dumslaff, T.; Feng, X.; Müllen, K.; Fasel, R.; *Nature*, **2016**, *531*, 489-492.

[2] Cai, J.; Ruffieux, P.; Jaafar, R.; Bieri, M.; Braun, T.; Blankenburg, S.; Muoth, M.; Seitsonen, A. P.; Saleh, M.; Feng, X.; Müllen, K.; Fasel, R. *Nature* **2010**, *466*-470.

[3] Peña, D.; Cobas, A.; Pérez, D.; Guitián, E.; *Synthesis*, **2002**, *10*, 1454-1458.

Thiol Grafted Imine-Based Covalent Organic Framework for Water Remediation Through Selective Removal of Hg(II)

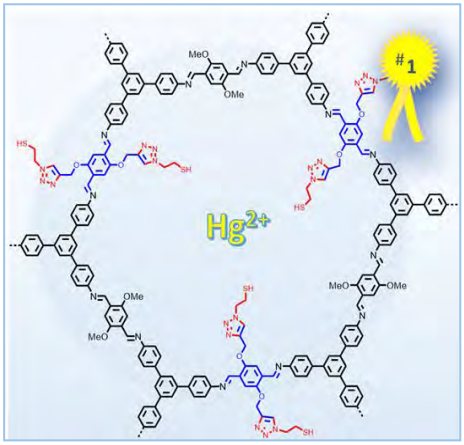
Laura Merí-Bofí, Sergio Royuela, José L. Segura, María José Mancheño

Departamento de Química Orgánica I, Facultad de C. Químicas, Universidad Complutense de Madrid, Madrid 28040, Spain

laumeri@ucm.es

***Keywords**: Covalent Organic Framewoks (COF), Hg(II) sorbents, Click Chemistry*

An imine-linked covalent organic framework[1] (**[HC≡C]$_{0.5}$-TPB-DMTP-COF**), endowed with reactive ethynyl groups on the walls of one-dimensional pores, has been used as a platform for pore-wall surface engineering with triazole and thiol groups to yield **TPB-DMTP-COF-SH**, which is suitable to interact very efficiently with mercury ions. The evaluation of the carefully designed **TPB-DMTP-COF-SH** is addressed as an effective and selective system for the detoxification of waters contaminated with mercury ions. The obtained results revealed an extraordinary capacity and a great efficiency of the polymeric material obtained with a very high distribution coefficient value K_d = 3.33 × 10^9. The **TPB-DMTP-COF-SH** retention value of Hg(II) from water is 99.98 % within 2 minutes and its record uptake capacity is 4,395 mg g^{-1} which represents the highest value reported so far. Thus, the level of mercury of a highly contaminated aqueous solution, 10 mg L^{-1} of Hg(II), is dramatically decreased within the limits of drinking water, upon treatment with **TPB-DMTP-COF-SH**. These results suggest that **TPB-DMTP-COF-SH** constitutes a very promising alternative for the remediation of contaminated spaces from an environmental perspective.



References:

[1] (a) Diercks, C. S.; Yaghi, Omar M. *Science* **2017**, *355*, 923. (b) Segura, J. L.; Mancheño, M. J.; Zamora, F. *Chem. Soc. Rev.* **2016**, *45*, 5635. (c) Huang, N.; Wang, P.; Jiang, D. *Nat. Rev. Mater.* **2016**, *1*, 16068. (d) Zhao, Y.; *Chem. Mater*. **2016**, *28*, 8079. (e a lle n a a, F.; Yaghi, O. M. *Acc. Chem. Res*. **2015**, *48*, 3053. (f) Ding, S. Y.; Wang W. *Chem. Soc. Rev*. **2013**, *42*, 548. (g) Colson, J. W.; Dichtel, W. R. *Nat. Chem.* **2013**, *5*, 453 .

Design and synthesis of new quinone derivatives against leishmaniasis

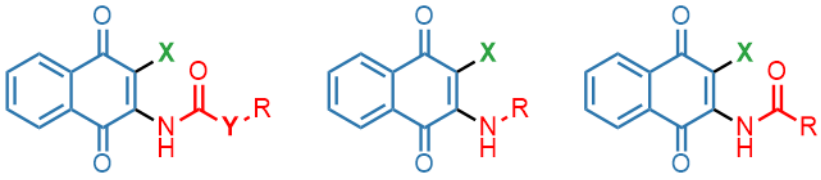
L. Nóvoa, V. Sebastián, C. Gil

Centro de Investigaciones Biológicas – CSIC, Ramiro de Maeztu, 9, 28040, Madrid, Spain
lunovoa@ucm.es

***Keywords**: quinones, leishmaniasis, neglected disease*

Leishmaniasis is the second protozoan disease in number of human affected, only superseded by malaria. The disease has a wide range of clinical pathologies produced by the infection with different protozoan species of the genus *Leishmania*, which are transmitted by the bite of infected female phlebotomine sandflies. Leishmaniasis is endemic in 98 countries associated with poverty. Globally, the disease accounts for 10-12 million people infected, with 1 million new cases per year.[1]
In spite of the high importance of leishmaniasis, currently available treatments are inadequate for their severe side effects and their resistance that is rising constantly, so investigation in this field is very important.

In this work, the search of new drugs for leishmaniasis was based on a phenotypic-based approach using different types of quinone derivatives which are well-known anti-parasitic agents due to their biological activity into the redox cycle.[2] Several benzoquinones with antileishmanial activity were recently tested in our research group and initial results on their mechanism of action supported the importance of the bioenergetic collapse of the parasite induced by these compounds. However, they suffer of low selectivity index (SI) leading to the design of new quinones that have been synthesized with the aim of increasing SI and therefore reducing their toxicity. The modifications include the introduction of ureas, carbamates or amides as substituents on the quinone scaffold.
The synthesis of new derivatives together with their biological evaluation will be here discussed.



X = Cl, H Y = O, N

References:
[1] Nagle, A. S.; Khare, S.; Kumar, A. B.; Supek, F.; Buchynskyy, A.; Mathison, C. J.; Chennamaneni, N. K.; Pendem, N.; Buckner, F. S.; Gelb, M. H.; Molteni, V. *Chem. Rev.* **2014**, *114*, 11305.
[2] Pinto, A. V., de Castro, S. L. *Molecules*, **2009**, *14*, 4570.

Síntesis y estudio de nanoestructuras híbridas fullereno-HPA

Pena C., Guitián, E.; Pérez, D.; Peña, D.

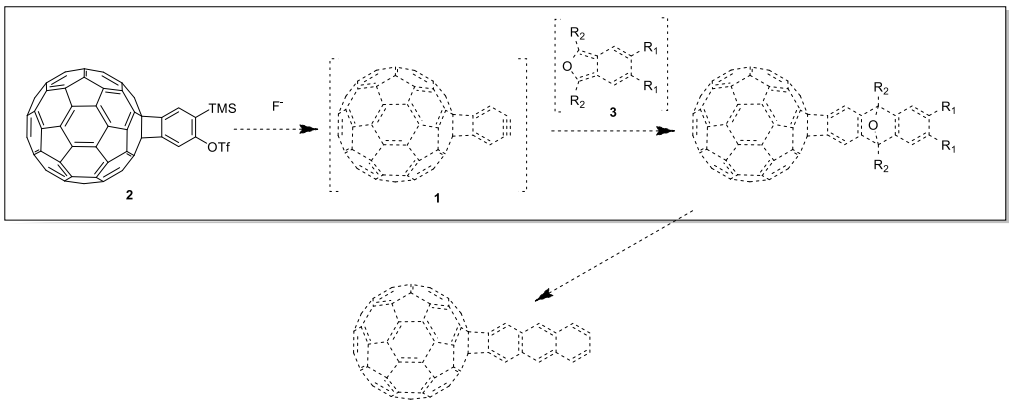
Departamento de Química Orgánica y Centro Singular de Investigación en Química Biológica y Materiales Moleculares (CiQUS), Universidad de Santiago de Compostela, C/ Jenaro de la Fuente s/n, 15782, Santiago de Compostela

celia.pena@rai.usc.es

***Keywords**: Arinos, fullereno, materiales moleculares.*

Los fullerenos, alótropos de carbono de forma esférica, se encuentran entre las familias de compuestos más estudiadas en el ámbito de los materiales moleculares.[1] Debido a su carácter aceptor de electrones se han utilizado en el desarrollo de híbridos dador-aceptor para células solares y otros sistemas electroactivos. Recientemente, en colaboración con el grupo del Prof. Nazario Martín (UCM), nuestro grupo de investigación ha descrito la generación del primer arino que incorpora una unidad de fullereno (*fullerobencino*,**1**) y su aplicación a la funcionalización covalente de grafeno.[2] Este novedoso *building block* tiene también utilidad para la síntesis de sistemas moleculares discretos de tamaño nanométrico con potencial utilidad en el campo de la electrónica molecular.

Se llevó a cabo la optimización del proceso de síntesis, purificación y aislamiento de un precursor del arino derivado de fullereno, el *fullerobencino* (**1**), previamente desarrollado en el grupo de investigación, y el ensayo de su cicloadición con sistemas diénicos reactivos como isobenzofuranos (**3**). El objetivo final, que continuará con el desarrollo del TFM, se dirige a la obtención de nuevos compuestos híbridos fullereno-aceno de interés en el campo de la electrónica molecular.



[1] A.Hirsch, *The Chemistry of the Fullerenes*, John Wiley & Sons,1-215.
[2] García, D.; Rodríguez-Pérez, L.; Herranz, M. A.; Peña, D.; Guitián, E.; Bailey, S.; Al-Galiby, Q.; Noori, M.; Lambert, C. J.; Pérez, D.; Martín, N. *Chem. Commun.* **2016**, *52*, 6667

PREPARATION OF CARBON QUANTUM DOTS BY PULSED LASER SYNTHESIS

S. Ramírez Barroso, D. García Fresnadillo, N. Martín

Department of Organic Chemistry, Faculty of Chemistry, Universidad Complutense de Madrid, 28040 Madrid, Spain
sergiram@ucm.es

Keywords: *carbon quantum dot, Nd-YAG pulsed laser, nanomaterial.*

A quantum dot is a nanometer-sized object (usually a semiconductor), where the excitons are confined in all three spatial dimensions. Inorganic semiconductor quantum dots (QDs) have attracted a huge interest owing to their unusual and interesting optoelectronic properties. However, the main disadvantages of QDs are their general intrinsic toxicity and the fact that they are colloids. On the other hand, carbon quantum dots (CQDs) are non-toxic, much easier to handle, and show the desirable optoelectronic properties of quantum dots, which makes them interesting candidates for a whole range of new applications.[1]

Despite this great potential, the main difficulty is still the production of high-quality CQDs, since current synthetic methods are either very harsh (not producing well-defined particles) or extremely inefficient. Therefore, a method allowing for the large-scale synthesis of CQDs, of well-defined size and chemical functionality, is still lacking and would certainly boost research and applications in this area.

In this project, a novel photochemical method for the preparation of luminescent CQDs has been studied using the first and second harmonic of a Nd-YAG pulsed laser, and following a bottom-up approach starting from different organic aromatic precursors.[2] The potential interest of this methodology has been demonstrated in terms of homogeneity and surface functionalization of the obtained products, very good availability of reagents and versatility of the technique.

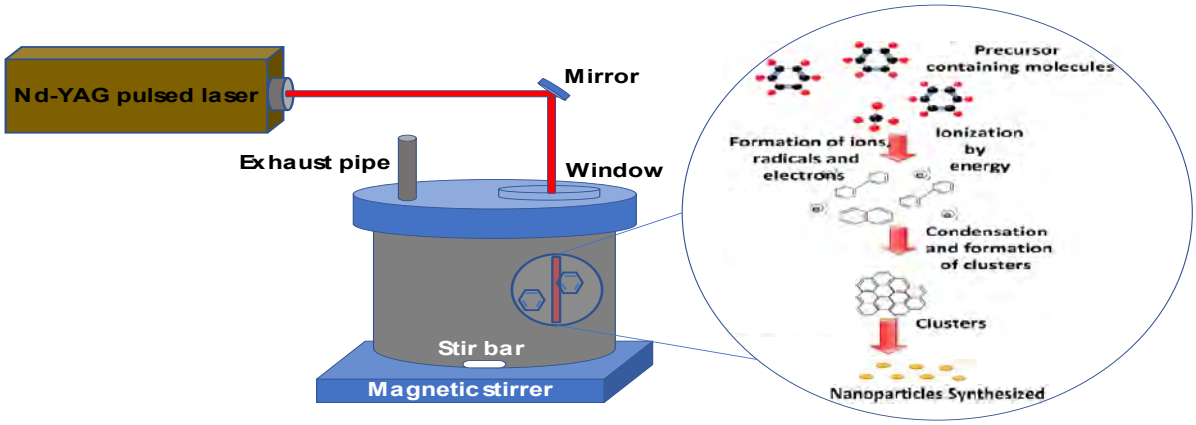


Fig.1. Detailed schematic of the experimental setup and the bottom-up approach mechanism for the syntesis of CQDs.[3]

References:

[1] Bacon, M.; Bradley, S.J.; Nann, T. *Part. Part. Syst. Charact.* **2014**, *31*, 415.
[2] Habiba, K.; Makarov, V.I.; Avalos, J.; Guinel, M.J.F.; Weiner, B.R.; Morell, G. *Carbon*. **2013**, *64*, 341.
[3] Habiba, K.; Makarov, V.I.; Weiner, B.R.; Morell, G. *Manufacturing Nanostrutures*. OCN, UK, 2014, 263.

Synthesis of Chiral Di(phenylethylene)s Derivatives as Precursors for New Helical Polymers

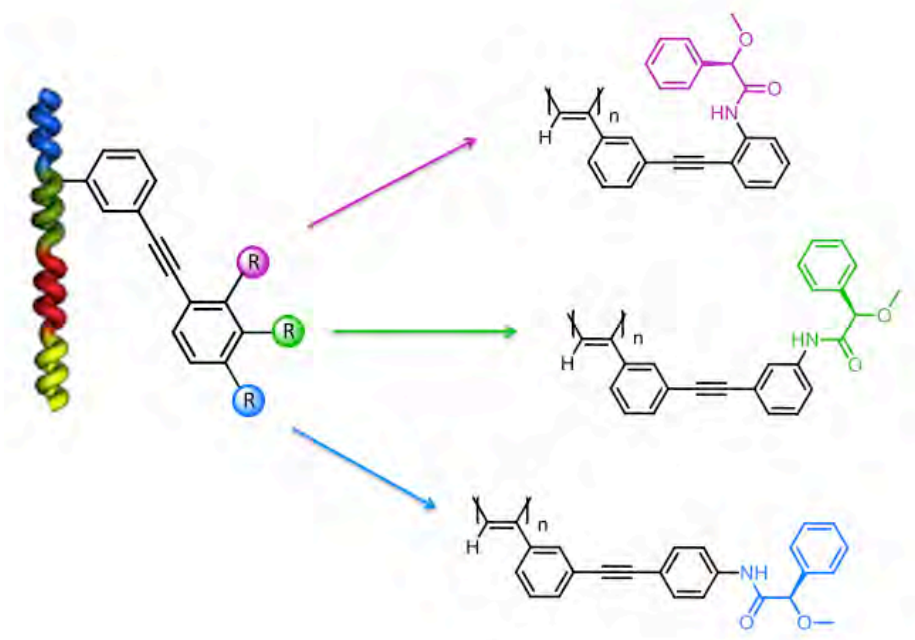
Elena Rivadulla, Félix Freire, Emilio Quiñoá

Centro de Investigación en Química Biolóxica e Materiais Moleculares, Universidade de Santiago de Compostela. C/Jenaro de la Fuente s/n; 15782, Santiago de Compostela, España;

elena.rivadulla@rai.usc.es

***Keywords**: PPAs, Chiral Helical Polymers*

The design, synthesis and structure elucidation of helical polymers with a predominant helix sense have been actively studied during the last decades. This attractive properties allow the application of this compunds in different fields such as material science, chemical sensing, asymmetric synthesis and separation of enantiomers. Poly(phenylacetylene)s (PPAs) are a type of dynamic helical polymers[1] that can be defined by two parameters: the helical sense of the helix, determined by AFM and Circular Dichroism (CD), and the helical pitch, that make the polymer more or less extended (conjugation of the double bonds), easily determined by CD/UV-Vis. In this work we decided to evaluate the effect caused by a rigid spacer introduced between the backbone and the pendant group. We have developed a new family of polymers derived from derived from MPA (α-methoxyphenylacetic acid), *ortho*-, *meta*- and *para*-substituted.



References:

E. Yashima, K. Maeda, H. Iida, Y. Furusho, K. Nagai, *Chem. Rev.*, **2009**, *109*, 6102.

Rodriguez, R.; Ignés-Mullol, J.; Sagués, F.; R., Quinoa, E.; Riguera, R.; Freire, F. Nanoscale, **2016**, *8*, 3362-3367

Félix Freire, Emilio Quiñoá, Ricardo Riguera. *Chem. Rev.* **2016**, *116*, *1242-1271*

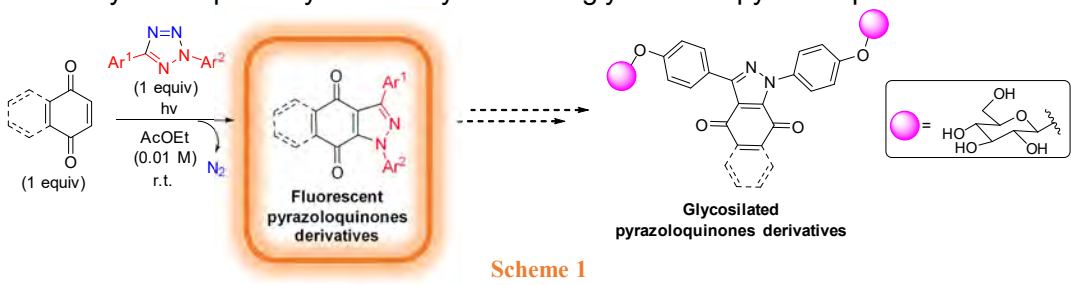
Synthesis of fluorescent glycosilated pyrazolquinones: 1,3-dipolar cycloaddition reactions between 2,5-diaryltetrazoles with quinones.

C. Rodríguez-Díaz, L. Ortiz-Rojano, I. Rodríguez Serna, J. Rojas-Martín, M. Ribagorda, M. C. Carreño.

Departamento de Química Orgánica, Universidad Autónoma de Madrid
ciro.rodriguez@estudiante.uam.es

***Keywords**: Quinones, tetrazoles, 1,3-dipolar cycloaddition*

The 1,3-dipolar cycloaddition reaction is a straightforward strategy that open access to 5-membered heterocyclic systems.[1,2] 2,5-Disubstituted tetrazoles can behave as masked dipoles species, that upon the exposure to UV light irradiation releases a nitrile imine dipole ready to react with different dipolarophiles to give pyrazoloquinones. This process, known as a photoclick 1,3-dipolar reaction, is considered as a valuable bioorthogonal transformation ideal for study biological processes.[3] Heterocyclic quinones are a group of naturally occurring quinones displaying a broad range of biological activities.[4] Our interest in extending synthetic applications of quinones,[5] prompted us to study a photoinduced 1,3-dipolar cycloaddition of 2,5-diaryltetrazoles with quinones as dipholarophiles, as a new route to synthesize the corresponding heterocyclic quinones.[6] The reaction gave direct access to a new family of fluorescent pyrazoloquinones in moderated to good yields (22-91%). Herein, we present our results towards the optimization of the reaction conditions for the photoclick reaction between naphthoquinones and diaryltetrazoles that improved the synthesis of pyrazoloquinones in terms of yield (50-95%) and irradiation times (2-14 h) (Scheme 1). Moreover the physical and chemical properties have been measured. Finally, in order to develop a fluorescent pyrazoloquinone compatible with biological systems and potentially living cells, we have proposed two synthetic pathways for the synthesis of glycosilated pyrazoloquinones.



Scheme 1

[1] Shu, W.-M.; Ma, Jun-R.; Zheng, K.-L.; Sun, H.-Y.; Wang, M.; Yang, Y.; Wu, A.-X. *Tetrahedron* **2014**, 70, 9321.
[2] a) Wang C, Chen X-H, Zhou S.-M.; Gong L-Z. *Chem. Commun*. **2010**, *46*, 1275. b) He, Z.; Liu, T.; Tao, H.;Wang, C.-J. *Org. Lett.*, **2012**, *14*, 6230.
[3] a) Wang Y., Song, W., Hu W. J., Lin Q. *Angew. Chem. Int. Ed*. **2009**, *48*, 5330. b) Yu Z., Ho l. Y., Lin Q. *J. Am. Chem. Soc*. **2011**, *133*, 11912. c) Li Z., Qian, L.; Li L., Bernhammer J. C., Huynh ,H. V., Lee, H-S.; Yao S. Q. *Angew. Chem. Int. Ed*. **2016**, *55*, 2002.
[4] Newsome, J. J.; Hassani, M.; Swann, E.; Bibby, J. M.; Beall, H. D.; Moody, C. J. *Bioorg. Med. Chem*. **2013**, *11*, 2999.
[5] For recent work see: a) del Hoyo, A. M.; Urbano, A.; Carreño M. C. *Org. Lett.* **2016**, *18*, 20. b) García-García, C.; Ortiz-Rojano, L.; Álvarez, S.; Álvarez, R.; Ribagorda, M.; Carreño, M. C. *Org. Lett.* **2016**, *18*, 2224.
[6] Tesis doctoral Jaime Rojas, **2017**, Universidad Autónoma de Madrid.

SEARCH OF NEW DREAM-LIGANDS AS POTENCIAL DREAM MODULATORS.

J. San Jacinto García, M. Gutiérrez-Rodríguez.

Instituto de Química Médica, CSIC, Madrid, Spain.
e-mail: jorge.sanjacinto@gmail.com, mgutierrez@iqm.csic.es

***Keywords**:DREAM, protein-protein interaction, Suzuki coupling.*

DREAM, also known as calsenilin or KChIP3, is a multifunctional calcium binding protein that controls the expression level and/or the activity of several proteins related to calcium homeostasis, neuronal excitability and neuronal survival[1]. This protein is widely expressed in the brain and, depending on the cell type and physiological conditions, shows multiple subcellular localizations, in the nucleus, cytosol or cell membrane[2]. In the last years, work from different laboratories has identified a growing list of interacting proteins that constitutes the DREAM interactome. Some of the protein-protein interactions (PPI) in which DREAM is involved, are related with neurodegenerative diseases such as DREAM/KV4 and DREAM/presenilins[1]. Recently, we have described the interaction between DREAM and the Activating Transcriptor Factor 6 (ATF6) and its role in the Huntington disease[3]. The discovery of small molecules capable of interacting with DREAM and modulate its interaction with other proteins involved in neurodegenerative processes, could open new avenues in the treatment of neurodegenerative diseases. During the last years, our research group has been working in the design and synthesis of novel DREAM-binding molecules, identifying promising DREAM-modulators[4]. Based on the structure-activity relationship established in our group, we have designed a new family of potential DREAM ligands. This new family of DREAM-ligands has been synthesized by a two-step methodology. The first step is the preparation of biphenyl intermediates by Suzuki coupling between organoboron derivatives and different aryl halides. The second step is the formation of an amide bond between the biphenyl intermediates and anilines with different pattern substitutions.

References:

[1]. a) Carrión, A.M.; Link, W.A.; Ledo, F.; Mellström, B.; Naranjo, J.R. Nature 1999, 398, 80. b) Buxbaum, J.D.; Choi, E.K.; Luo, Y.; Lilliehook, C., Crowley, A.C.; Merriam, D.E., Wasco, W. Nat. Med. 1998, 4, 1177. c) An, W.F; Bowlby, M.R.; Betty, M., Cao, J.; Ling, H.P.; Mendoza, G.; Hinson, J.W.; Mattsson, K.I; Strassle, B.W.; Trimmer, J.S.; Rhodes, K.J. Nature. **2000**, *403*, 553.
[2]. Mellström, B.; Savignac, M.; Gomez-Villafuertes, R.; Naranjo, J. R. Physiol. Rev. **2008**, *88*, 4213.
[3]. Naranjo, J.R.; Zhang, H.; Villar, D.; González, P.;Dopazo, X.M.; Morón-Oset, J.; Higueras, E.; Oliveros, J.C.; Arrabal, M.D.; Prieto, A.; Cercós, P.; González, T.; De la Cruz, A.; Casado-Vela, J.; Rábano, A.; Valenzuela, C.; Gutierrez- Rodriguez, M.; Li, J. Y.; Mellström, B. J. Clin. Invest. **2016**,*126*, 627.
[4]. Gutiérrez Rodríguez, M.; Cercós Pita, P.; Martín Martínez, M.; Herranz, R.; García López, M. T.; Valenzuela Miranda, M. C.; Naranjo Orovio, J. R.; Mellstrom, B.; Dopazo Santos, J. M.; González Pérez, P. Compuestos moduladores del sensor neuronal de calcio DREAM y sus usos terapéuticos. PCT2015/070923.

Ciclaciones borilativas catalizadas por Fe.

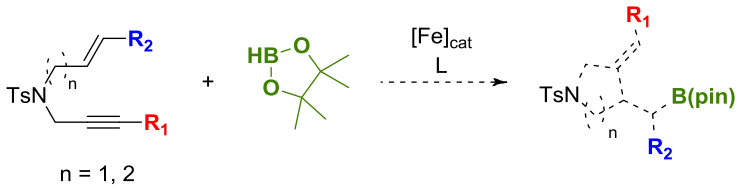
P. Rodríguez-Salamanca, N. Cabrera-Lobera, Diego J. Cárdenas.

Departamento de Química Orgánica, Facultad de Ciencias, Universidad Autónoma de Madrid.
patricia.rodriguezs01@estudiante.uam.es

***Palabras clave**: ciclación borilativa, hierro, eninos.*

Las reacciones de ciclación borilativa son de interés al permitir la creación de carbo- y heterociclos por formación de enlaces C-C y C-B en un único paso de reacción. Además, la incorporación de un derivado de boro en la estructura tiene especial relevancia por su baja toxicidad y su compatibilidad con diferentes grupos funcionales, además de su indudable versatilidad sintética.[1] Sin embargo, la síntesis tradicional de este tipo de derivados requiere el uso de condiciones de reacción severas, como altas temperaturas, disolventes tóxicos y catalizadores caros y no respetuosos con el medio ambiente, como el paladio[2] o el cobre[3].

Así, describimos la primera ciclación borilativa de eninos (derivados de tosilamidas) catalizada por Fe con pinacolborano. Este trabajo se centra en el estudio del efecto de diferentes grupos tanto dadores como aceptores de carga en la cadena propargílica, y el efecto de un alqueno terminal o interno. Resultados preliminares sugieren que esta estrategia presenta un elevado potencial sintético y proporciona un enfoque eficiente a la construcción de derivados de pirrolidinas utilizando condiciones más suaves a las utilizadas hasta ahora. La presencia de un resto pinacolborano en la estructura es particularmente importante debido a su facilidad para una posterior funcionalización a través de la reacción de acoplamiento tipo Suzuki-Miyaura o reacciones de oxidación, entre otras.



n = 1, 2

Referencias:

[1] Xu, L.; Zhang, S., Li, P., *Chem. Org. Rev.*, **2015**, *44*, 8848 - 8858.

[2]: a) Marco-Martínez, J.; López-Carrillo, V.; Buñuel, E.; Simancas, R.; Cárdenas, D.J., *J. Am. Chem. Soc.*, **2007**, *129*, 1874 - 1875; b) Pardo-Rodríguez, V.; Buñuel, E.; Collado-Sanz, D.; Cárdenas, D.J., *Chem. Commun.*, **2012**, *48*, 10517 - 10519; c) López-Durán, R.; Martos-Redruejo, A.; Buñuel, E.; Pardo-Rodríguez, V.; Cárdenas, D.J., *Chem. Commun.*, **2013**, *49*, 10691 - 10693.

[3]: Xi, T.; Lu, Z., *ACS. Catal.*, **2017**, *7*, 1181 - 1185.

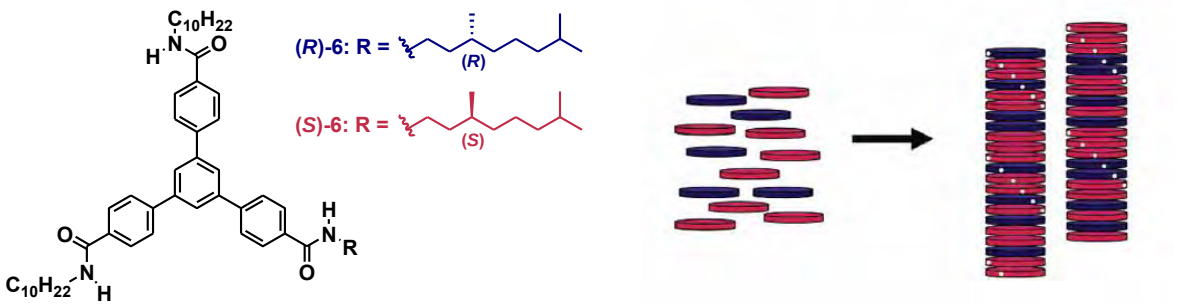
AMPLIFICATION OF CHIRALITY IN TRICARBOXAMIDE TRIPHENYLBENZENE-BASED SUPRAMOLECULAR POLYMERS

R. Sánchez-Naya, Y. Dorca, R. Gómez, L. Sánchez

Grupo de Moléculas Anfifílicas y Polímeros Supramoleculares
Departamento de Química Orgánica I. Facultad de CC. Químicas
robsan01@ucm.es

***Keywords**: Amplification of chirality, supramolecular polymers, majority rules*

In this work, disc-shaped asymmetrical 1,3,5-triphenylbenzene derivatives, **(*R*)-6** and **(*S*)-6**, endowed with peripheral amide moieties have been synthetized and their ability to experience amplification of chirality has been investigated. These compounds undergo a supramolecular polymerization induced by the operation of *H*-bonding interactions between the amide functional groups and π-π stacking between the aromatic moieties.[1] The ability of tricarboxamides **(*R*)-6** and **(*S*)-6** to self-assemble has been studied by ^{1}H-NMR at variable concentration and circular dichroism (CD). This technique was also used to assess the transfer of chirality from the molecular building blocks to the supramolecular aggregate. In addition, CD leads to the elucidation of the cooperative supramolecular polymerization mechanism and the main thermodynamical parameters of this process. Finally, a "majority rules" experiment was carried out to explore the influence of the stereogenic center on chiral amplification phenomena.[2] The results presented herein contribute to shed light on the puzzling origin of homochirality.



References:
[1] Aparicio, F.; García, F.; Sánchez, L. *Encyclopedia of Polymer Science and Technology* (Ed.: M. Peterca), John Wiley & Sons, Inc., **2012**.
[2] a) García, F.; Sánchez, L. *J. Am. Chem. Soc.* **2012**, *134*, 734 b) Smulders, M. M. J.; Filot, I. A. W.; Leenders, J. M. A.; Schoot, P.; Palmans, A. R. A.; Schenning, A. P. H. J; Meijer, E. W. *J. Am. Chem. Soc.* **2010**, *132*, 611.

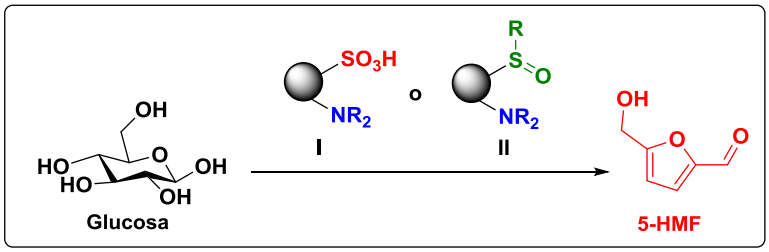
Síntesis de nuevos organocatalizadores bifuncionales para la transformación de la biomasa.

Mercedes Sánchez, Irene Martín, Alejandro Parra*y Mariola Tortosa[a]
[a]*Departamento de Química Orgánica, Universidad Autónoma de Madrid, Av. Francisco Tomás y Valiente 7, Madrid, Spain*

e-mail: mercedes.sanchezgalan@estudiante.uam.es

***Keywords**: 5-HMF, biomasa, organocatálisis*

Los combustibles fósiles se han convertido en las principales fuentes de carbono y energía de la sociedad actual. Debido a que presentan diversos problemas como emisiones de gases invernaderos o la escasez de las reservas es necesaria la búsqueda de alternativas. Actualmente existen diferentes fuentes de energía, pero el nuevo reto para los científicos es la búsqueda de una fuente de carbono que sustituya al petróleo[1]. En este contexto, el 5-hidroximetilfurfural (5-HMF) es la principal alternativa. Éste se obtiene por transformación de la glucosa (principal componente de la biomasa) en un proceso de dos etapas: isomerización de glucosa a fructosa, proceso catalizado por bases y la posterior deshidratación de la fructosa catalizada por ácidos y por disolventes polares apróticos como el DMSO.[2] La organocatálisis, el uso de pequeñas moléculas orgánicas como catalizadores, ha sido escasamente utilizada en la transformación de la biomasa.[3] De esta forma, se ha llevado la síntesis de diferentes familias de organocatalizadores bifuncionales amino-ácido y aminosulfóxido. Además, se ha estudiado la actividad catalítica de estos catalizadores y diferentes aminoácidos, en la transformación de la D-glucosa a 5-HMF usando diferentes disolventes.



References:
[1] Gallezot, P. *Chem. Soc. Rev.* **2012**, *41*, 1538.
[2] Anandam, S.; Amarasekara, T.D.; Williams, C. C.; Ebede. *Carbohydrate Research.* **2008**, *343*, 3021.
[3] Liu, D. (D. J); Chen, E. Y.-X- *Green. Chem.* **2014**, *16*, 964.

Synthesis of porphyrins for their application in perovskite solar cells

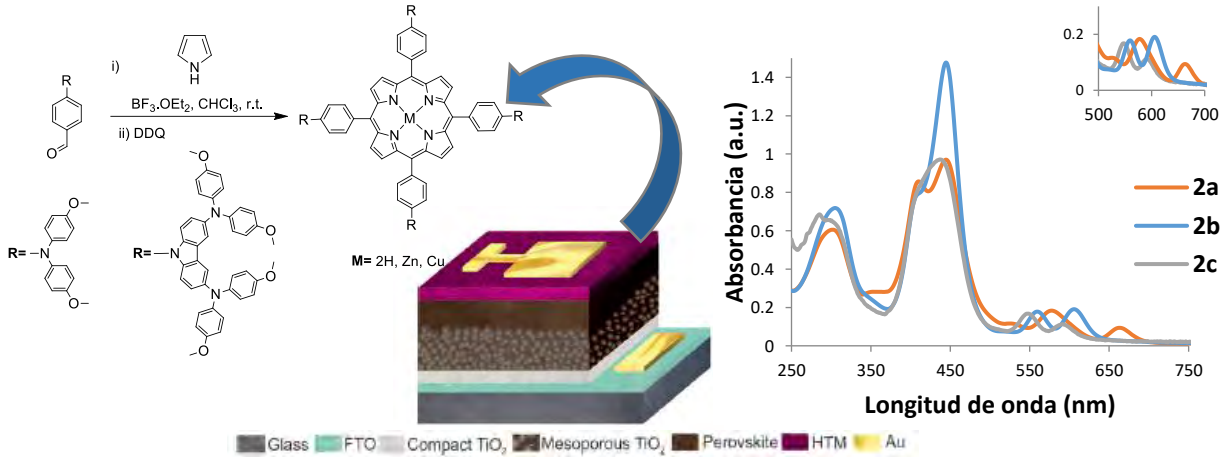
P. Simón Marqués,G. de la Torre

Departamento de Química Orgánica, Facultad de Ciencias, Universidad Autónoma de Madrid, Cantoblanco 28049-Madrid

e-mail: pablo.simonm@estudiante.uam.es

***Keywords**: porphyrin, hole-transporting material, perovskite solar cells.*

The need to set renewable energies as the principal energy sources is evident and, within these emerging energies, photovoltaics play an important role. Nowadays, silicon-based panels are the most widespread used, but many disadvantages like their fabrication process are promoting the research in new devices, where perovskite solar cells (PSCs) have the highlights. In addition to the perovskite photosensitizer, these solar cells require a hole transporting material (HTM) to make the transfer of charge more efficient. Looking for alternatives to Spiro-OMeTAD, the most common HTM employed to date, phtalocyanines and porphyrins[1] arise as interesting targets due to their electron-donor character, high hole transport capabilities and stability. In particular, certain porphyrin-based perovskite cells have reached efficiencies closer to MAPbI3/Spiro-OMeTAD devices.[2] In this work, new porphyrins have been synthesized for their application in PCSs. Diphenylamines and carbazol substituents have been attached to metal free, Zn(II) and Cu(II) *meso*-tetraphenyl porphyrin skeletons, to study the influence of these donor groups and the different atoms inside the cavity on the HOMO levels of the chromophores, and on the crystallinity of the films prepared with these molecules, both factors being fundamental to determine the final efficiency of the device. The target porphyrins were obtained in a convergent synthesis via Lindsey's condensation of the precursor aldehydes. Photophysical and electrochemical studies indicated that HOMO energy levels of the molecules are optimum to induce the hole transfer from the porphyrin film to the perovskite.



[1] Calió, L.; Amrana Kazim, S.; Grätzel, M.; Ahmad, S. *Angew. Chem. Int. Ed.* **2016**, *551*, 4522.
[2] Chou, H.-H.; Chiang, Y.-H.; Li, M.-H.; Wei, H.-J.; Mai, C.-L.; Chen, P.; Yeh, C.-Y. *ACS Energy Lett.* **2016**, *1*, 956.

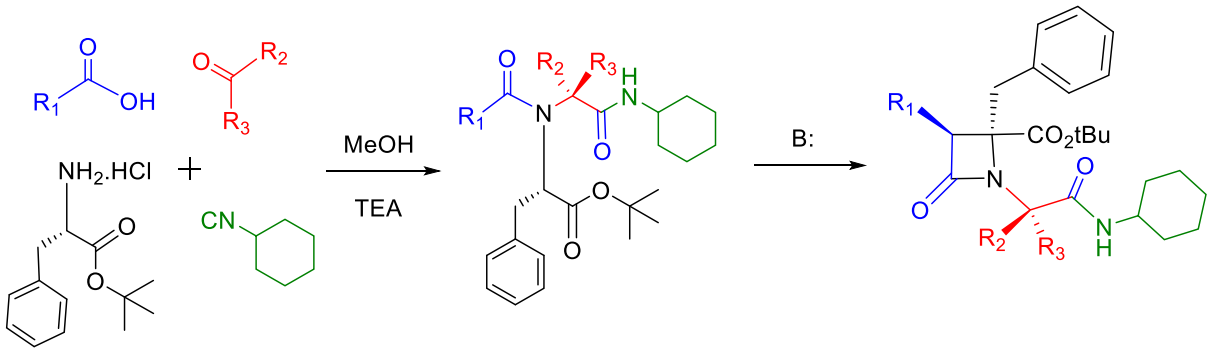
Combination of Ugi reactions and cyclization processes for the synthesis of new highly functionalized β-lactams

C. Sánchez-Cid Muñoz, R. González-Muñiz

Instituto de Química Médica (IQM-CSIC), Juan de la Cierva 3, 28006 Madrid
e-mail: crists04@ucm.es

***Keywords**: Ugi reaction, base-mediated cyclization, β-lactams*

β-Lactams are of main interest in medicinal chemistry, not only as antibiotics, as the central scaffold for antitumor, antiviral, and cholesterol lowering agents, among others.[1], [2]
As key intermediates to obtain new highly substituted β-lactams with potential biological interest, in this work we will explore the combination of Ugi reactions from α-aminoesters, followed by base-promoted cyclization of the linear adducts. [3], [4], [5]
Starting from H-Phe-O^{t}Bu and cyclohexyl isocyanide, we have investigated the scope of the Ugi reaction using various carbonyl compounds, both aldehydes and ketones, and different carboxylic acids, suitably decorated to allow nucleophilic substitution or Michael addition of the enolates generated in basic media.
This procedure allows us to prepare highly functionalized monocyclic β-lactams **2** in a regio- and stereoselective manner.



References:

[1] Bonfiglio, G.; Russo, G.; Nicoletti, G. *Exp. Opin. Inv. Drug.* **2002**, *11*, 529 – 544.
[2] Pérez-Faginas, P.; Aranda, M. T.; González-Muñiz, R. An Update on the Synthesis of β-Lactams. *Curr. Org. Synth.* **2009**, 6, 325-341.
[3] Ugi, I.; Meyr, R.; Fetzer, U.; Steinbrückner, C. *Angew. Chem.* **1959**, *71*, 386 – 388.
[4] Wehlan, H.; Oehme, J.; Scäfer, A.; Rossen, K. *Org. Process Res. Dev.* **2015**, 19, 1980 –1986.
[5] Pérez-Faginas, P.; O'Reilly, F.; O'Byrne, A.; García-Aparicio, C.; Martín-Martínez, M.; Pérez de Vega, M. J.; García-López, M. T.; González-Muñiz, R. *Org. Lett.,* **2007,** *9,* 1593-1596.

Controlled Polymerization of Self-assembled Cyclic Peptide Nanotubes for Bundle Formation

L. Suárez Barrigón, A. Méndez Ardoy, J. R. Granja Guillán, J. Montenegro García

Departamento de Química Orgánica, Centro Singular de Investigación en Química Biolóxica e Materiais Moleculares (CIQUS), Universidade de Santiago de Compostela, 15782, Santiago de Compostela, Spain
e-mail: leticia.suarez.barrigon@rai.usc.es

Keywords: *supramolecular, nanotube, cyclic peptide*

It is well known that the integrity of cell membranes is maintained by the cytoskeleton. This is a unique scaffold formed by several structural proteins that can modulate the shape of the cell and its inner molecular transport. These processes are of extremely importance for the cell viability.[1] From previous work of our research group we know that it is possible to form supramolecular nanotubular structures from cyclic peptides of alternating chirality that self-assemble on top of each other by hydrogen bonded networks.[2] The objective of this work is to control the supramolecular polymerization of cyclic peptides by the external manipulation of the media conditions. We will initially focus on controlling the polymerization-depolymerization process by pH changes and redox chemistry.

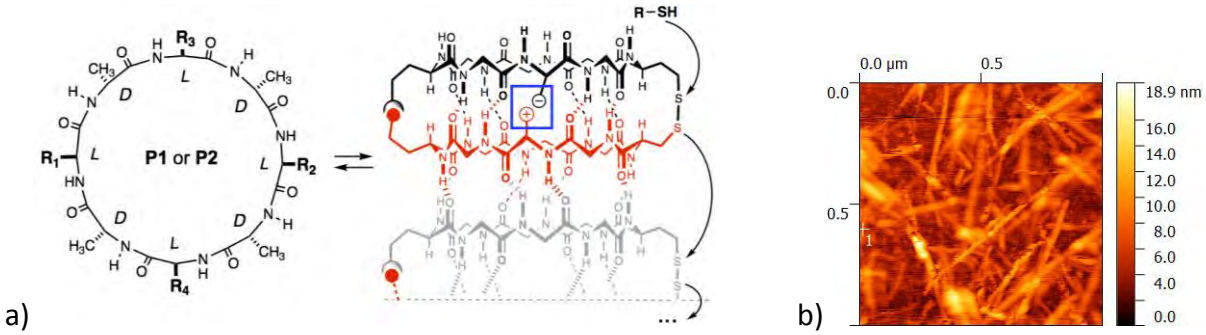


Figure 1. a) Formation of nanotubes induced by several stimuli like pH changes or disulfide bond formation. b) AFM image showing the formation of nanotubes under specific pH conditions after gelation of the cyclic peptide in HEPES buffer.

References

[1] A. P.Liu, D. A. Fletcher. *Nat. Rev. Mol. Cell Biol.***2009**, *10*, 644–650.

[2] J. Montenegro, C. Váquez-Vázquez, A. Kaylin, K. E. Geckeler, J. R. Granja. *J.Am. Chem. Soc.***2014**,*136*, 2484-2491.

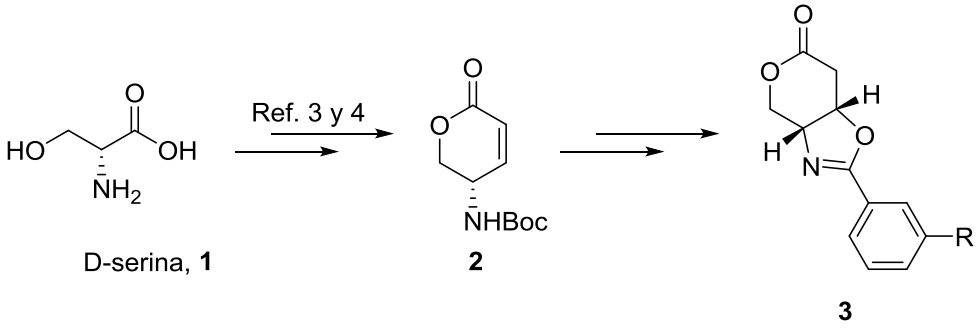
SYNTHESIS AND DEVELOPMENT OF NEW ^{18}F-PET RADIOTRACERS

A. Torres, A. M. González Fuente, F. Sánchez-Sancho*, A. García Csàkÿ*

Medicinal Chemistry Institute, Spanish National Research Council (CSIC), Juan de la Cierva 3, 28006, Madrid, Spain
Pluridisciplinar Institute, Complutense University of Madrid, Paseo Juan XXIII 1, 28040, Madrid, Spain
e-mail: altorresruiz@gmail.com

***Keywords**: tau, Alzheimer, radiotracer*

Neurodegenerative diseases affect millions of people around the world. One set of these are the so-called tauopathies, which are characterized by abnormal aggregation of the tau protein. The best known is Alzheimer's disease (AD). When tau is hyperphosphorylated, it forms paired helical filaments (PHFs) which have been identified in the neurofibrillary tangles (NFTs), which are a hallmark in the AD brain. These tangles are pathological because they prevent the neuron from carrying out its correct function.[1] In this work, a series of structures have been proposed to evaluate its affinity for tau protein, in order to design new radiotracers to monitor *in vivo* the evolution of this type of diseases by Positron Emission Tomography (PET). Thanks to the labeling of this protein we could understand the mechanisms and development of the disease, and most important, the diagnosis in the early stages for the application of an efficient treatment, because normally, the disease is detected in very advanced stages when the treatments are not effective.[2]



D-serina, **1** **2** **3**

***Scheme 1.** Synthesis of a candidate for ^{18}F-PET radiotracer*

References:

[1] Iqbal, K.; Liu, F.; Gong, C.-X. *Nat. Rev. Neurol.* **2016**, *12* (1), 15. [2] Oukoloff, K.; Cieslikiewicz-Bouet, M.; Chao, S.; Da Costa Branquinho, E.; Boutellier, C.; Jean, L.; Renard, P.-Y. *Curr. Med. Chem.* **2015**, *22*, 3278. [3] Dondoni, A., Perrone, D. *Org. Synth.* **2000**, *77*, 64. [4] Miwa, H.; Hashimoto, K.; Shirahama, H. *Tetrahedron* **1996**, *52* (6), 1931.

Antitumoral Oligocationic Peptides Bearing 2,2'-Bipyridine Ligands

Sonia Boga[1], M. Eugenio Vázquez Sentís[1], Miguel Vázquez Lopez[2]

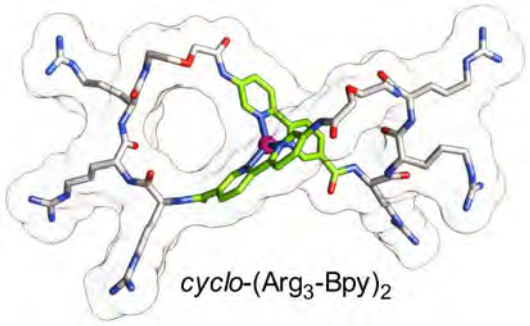
[1] *Centro Singular de Investigación en Química Biolóxica e Materiais Moleculares (CIQUS) and Departamento de Química Orgánica, Universidade de Santiago de Compostela, 15782 Santiago de Compostela (Spain).*

[2] *Centro Singular de Investigación en Química Biolóxica e Materiais Moleculares (CIQUS) and Departamento de Química Inorgánica, Universidade de Santiago de Compostela, 15782 Santiago de Compostela (Spain).*

sonia.boga@rai.usc.es

***Keywords**: Peptides, Anticancer, Coordination Chemistry*

The antitumoral effect of metal-chelators has been traditionally attributed to their ability to sequester metal ions. However, disruption of redox homeostasis, has gained increased attention.[1] Thus, the antitumoral elesclomol transports extracellular Cu(II) into the mitochondria, where it is reduced to Cu(I) and catalyzes the generation of toxic Reactive Oxidative Species (ROS).[2] We present the synthesis and characterization of the cyclo-(Arg3-βAlaBpy)2 (**1c**). Peptide was obtained following standard solid-phase peptide synthesis (SPPS) protocols, using the Fmoc-protected 2,2'-bipyridine derivative (Fmoc-βAlaBpy-OH) as chelating unit,[3] after cyclization of a side chain-protected intermediate in solution and subsequent deprotection with an acidic TFA cocktail. The metal binding properties were studied by fluorescence spectroscopy by titrating increasing concentrations of selected metal ions into solutions of peptide **1c**, while monitoring the emission of the 2,2'-bipyridine ligand (λ_{exc} = 305 nm/λ_{emiss} = 420 nm). The titration profiles were then fitted to 1:1 or mixed 1:1/1:2 models using the DynaFit software,[4] yielding in all cases high-affinity complexes with KDs in the low μM range (e.g., KD(1:1) 1c/Fe(II) ≈ 8 μM; KD(1:2) **1c**/Cu(II) ≈ 2 μM).



We thank the support given by the Spanish grants CTQ2015-70698-R, the Xunta de Galicia GRC2013-041, and Centro Singular de investigación de Galicia accreditation 2016-2019, ED431G/09.

References:

[1] W.-Q. Ding, S.E. Lind, (2009) IUBMB Life 61:1013–1018.

[2] M. Nagai, N.H. Vo, L. Shin Ogawa, D. Chimmanamada, T. Inoue, J. Chu, B.C. Beaudette-Zlatanova, R. Lu, R.K. Blackman, J. Barsoum, K. Koya, Y. Wada, (2012) Free Radic. Biol. Med. 52:2142–2150.

[3] I. Gamba, G. Rama, E. Ortega-Carrasco, J.-D. Maréchal, J. Martínez-Costas, M. Eugenio Vázquez, M.V. López, (2014) Chem. Commun. 50:11097–11100.

[4] P. Kuzmic, (1996) Anal. Biochem. 237:260–273.

Iodinated BODIPY photosensitizers for $^1O_2$ production

Gabriela Cantero, Ana B. Descalzo, Guillermo Orellana

Dpto. Química Orgánica. Fac. Química. Av. Complutense s/n – 28040 - Madrid
E-mail: gabrielacantero@ucm.es

***Keywords**: BODIPY dyes, singlet oxygen, photodynamic therapy.*

Leishmania parasites are responsible for a disease known as Leishmaniasis, that affects mainly developing tropical and subtropical areas of the Western Hemisphere, Asia, Africa and South America. Cutaneous leishmaniasis is a dermatological condition that shows up on the skin surface and is suitable to be treated by photodynamic therapy (PDT) (Akilov *et al.*, 2011). This treatment relies in the effect caused by singlet oxygen ($^1O_2$), which is generated from ground state oxygen ($^3O_2$) upon illumination in the presence of a photosensitizer. Singlet oxygen is a very reactive (strongly oxidant) molecule able to induce cell death.

The aim of this project is to develop BODIPY (boron-dipyrromethene) photosensitizers that meet the conditions required for treating the adverse skin reaction caused by Leishmania parasites. These conditions include a high quantum yield of $^1O_2$ production and absorption of light in the so called “biological window”, a spectral range covering the 650-900 nm interval. The last avoids most spectral interferences present in biological samples, improving PDT yield by increasing penetration depth of light into the skin. To achieve these objectives, a BODIPY core will be chemically modified as follows: i) heavy atoms (iodine) will be inserted in the structure in order to enhance the intersystem crossing rate and, therefore, the singlet oxygen production (Zhou *et al.*, 2012) and, ii) extension of the conjugated π-system via condensation of two styryl groups to the BODIPY core will yield sensitizers absorbing at longer wavelengths (Rurack *et al.* 2001). In this work, the synthesis of a novel near-infrared absorbing BODIPY dye is described, along with its spectroscopic characterization, proving that the selected dye is a promising candidate for its application in PDT.

References:

1. Akilov, O. E.; Sallum, U. W.; Hasan, T. PDT for cutaneous leishmaniasis. *Compr. Ser. Photochem. Photobiol. Sci.* **2011**, *11*, 303–326.
2. Zhou, L.; Wei, S.; Ge, X.; Zhou, J.; Yu, B.; Shen, J. External Heavy-Atomic Construction of Photosensitizer Nanoparticles for Enhanced in Vitro Photodynamic Therapy of Cancer. *J. Phys. Chem. B* **2012**, 116, 12744–12749.
3. Rurack, K.; Kollmannsberger, M.; Daub, J. A highly efficient sensor molecule emitting in the near infrared (NIR): 3,5-distyryl-8-(p-dimethylaminophenyl)difluoroboradiaza-s-indacene. *New. J. Chem.* **2001**, *25*, 289–292.

NEW FLUORESCENT GLYCOPROBES FOR BIOLOGICAL APPLICATIONS

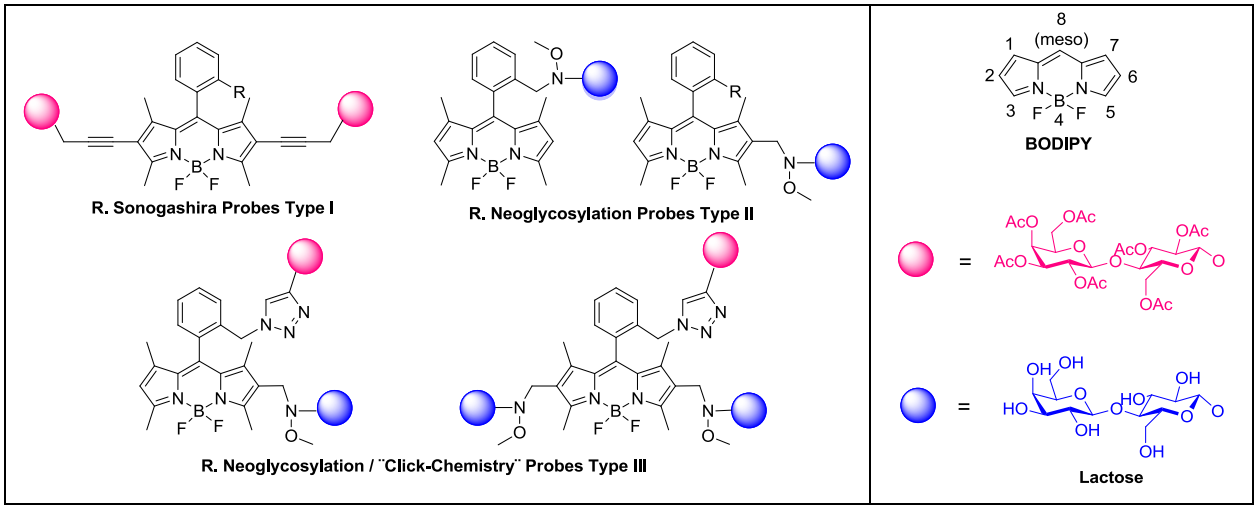
L. Díaz, A. M. Gómez, J. C. López

Instituto de Química Orgánica General, IQOG-CSIC*, Juan de la Cierva 3, 28006-Madrid*
ladi01@ucm.es

***Keywords**: Soluble BODIPYs, Carbohydrates, Glycoprobes.*

Difluoroboron dipyrromethene (4,4-difluoro-4-bora-3*a*,4*a*-diaza-*s*-indacene) derivatives or BODIPYs, (see Figure), constitute a family of fluorescent dyes that have attracted considerable interest in the last years.[1] In this context, we have been interested in the combination of carbohydrates with BODIPYs to obtain "glycoprobes",[2,3] which will display enhanced biocompatibility and water-solubility. To tackle this approach we have been screening: *i)* the nature of the covalent carbohydrate-BODIPY ligation, *ii)* the (BODIPY) position(s) of the ligation, and *iii)* the nature (and number) of the carbohydrates involved.

Three types of covalent ligations have been studied, arising from: *a)* Sonogashira coupling of BODIPY-iodides and carbohydrate-alkynes (**Type I**), *b)* neoglycosylation of BODIPY methoxyamines with saccharides (**Type II**), and *c)* a combination of CuAAC-type click reactions of BODIPY azides and neoglycosylation (**Type III**). The implementation of these methods have allowed the preparation of a variety of carbohydrate-BODIPY hybrids, some of which are displayed in the Figure below.



[1] (a) Ulrich, G., Ziessel, R., Harriman, A., Angew. *Chem., Int. Ed*. **2008**, *47*, 1184; (b) Loudet, A., Burgess, K., *Chem. Rev*. **2007**, *107*, 4891.
[2] Abellán, M., García, M. I., Ortiz, C., García, J. M., Nierengarten, J., Vincent, S.P., *Eur. J. Chem,*. **2016**, *22*, 1.
[3] (a) Lobo, F., Gómez, A. M., Miranda, S., Lopez, J. C., *Chem. Eur. J.* **2014**, *20*, 10492. (b) Rio, M., Lobo, F., Cristobal, J. C., Oliden, A., Bañuelos, J., Lopez-Arbeloa, I., García-Moreno, I., Gomez, A. M., *J. Org. Chem.*, **2017**, *82* (2), 1240.

Adiciones 1,4 Organocatalíticas de Cetiminas Derivadas de Glicina a Nitroalquenos

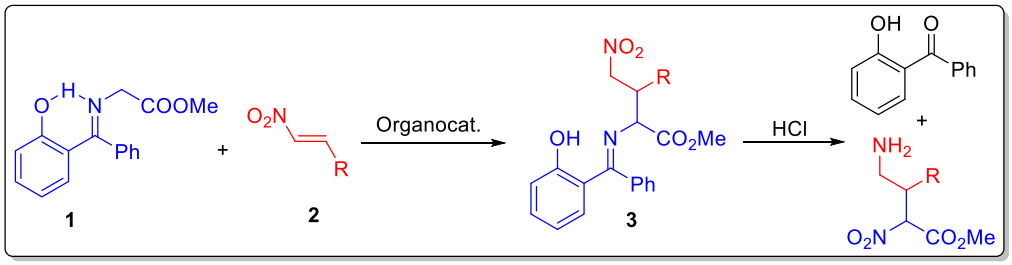
Manuel Iniesta Bernabé, Francisco Esteban, Andrea Guerrero, Mario Parra, Alberto Fraile, José Alemán

Departamento de Química Orgánica, Módulo 1, Universidad Autónoma de Madrid, Madrid-28049, España
e-mail: manuel.iniesta@estudiante.uam.es

***Palabras clave**: Organocatálisis, adición Michael, enantioselectividad.*

Los α,γ-aminoácidos se encuentran en una gran cantidad de distintos productos naturales[1a] y productos farmacológicos con actividad biológica.[1b] Éstos pueden ser sintetizados de forma sencilla a partir de derivados de α-iminoésteres. Hasta la fecha, la ruta más común para la síntesis de α-iminoésteres quirales es la adición asimétrica tipo Michael de cetiminas derivadas de la glicina a nitroalquenos catalizada por metales.[2] Sin embargo, la versión organocatalítica de esta reacción no ha podido ser llevada a cabo hasta el momento por la baja reactividad de las cetiminas derivadas **1**.[3]

En esta comunicación presentamos la primera aproximación organocatalítica altamente enantioselectiva para la síntesis de una gran variedad de α-iminoésteres derivados **3** con buenos rendimientos (75-86%) y excelentes excesos enantioméricos (89-97% ee) a través de una adición tipo Michael de las cetiminas **1** anitroalquenos **2** catalizada por la tiourea de Takemoto (Esquema 1).



Esquema 1

La presencia del grupo hidroxilo en la cetimina es esencial para que exista reactividad, ya que este grupo provoca un aumento de la acidez de los hidrógenos metilénicos debido a la formación de un enlace de hidrógeno intramolecular, haciendo posible la formación del iluro intermedio en presencia del organocatalizador bifuncional de Takemoto. Adicionalmente el grupo hidroxilo ejerce un papel crucial en el control estereoselectivo de la reacción. Finalmente, cabe destacar que la hidroxilcetona, auxiliar químico de la reacción, puede recuperarse tras la hidrólisis de la cetimina en un buen rendimiento.

Referencias:

1. (a) O. M. Berner, L. Tedeschi, D. Enders, *Eur. J. Org. Chem*. **2002**, 1877. b) Y. Huang, Q. Li, T. -L. Liu, P. -F. Xu, *J. Org. Chem*. **2009**, *74*, 1252.
2. K. Imae, T.Konno, K. Ogata, S. Fukuzawa, *Org. Lett.* **2012**, *14*, 4410.
3. J. Xie, K. Yoshida, K. Takasu, Y. Takemoto, *Tetrahedron Lett.* **2008**, *49*, 6910.

APROXIMACIÓN A SECUENCIAS DE CICLACIÓN/ACOPLAMIENTO RADICÁLICO CATALIZADAS POR NÍQUEL.

C. Izquierdo García, A.M. Martín Castro.

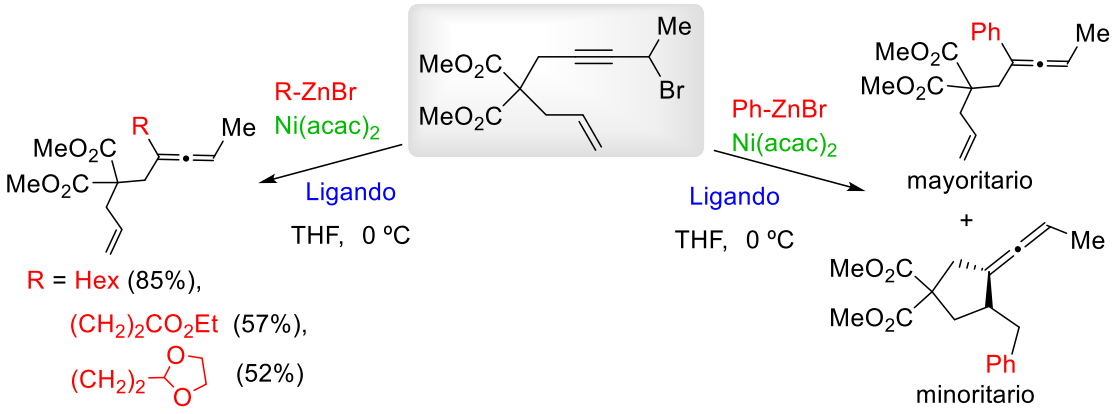
Universidad Autónoma de Madrid

carolina.izquierdog @estudiante.uam.es

***Keywords**: (vinilidenciclopentanos, catálisis, níquel)*

Numerosos compuestos biológicamente activos presentan un grupo funcional de tipo 1,2-dienilo (aleno), herramienta sintética muy útil en Química Orgánica debido al elevado número de transformaciones que puede experimentar. Dentro de los compuestos alénicos, el subgrupo de vinilidencicloalcanos merece especial mención debido a su amplia presencia en la naturaleza[1]. Las características intrínsecas de los alenos han determinado el desarrollo de nuevas metodologías sintéticas catalíticas para abordar su preparación. Recientemente se ha descrito la síntesis de alenos a partir de bromuros propargílicos y bromuros de alquilzinc en presencia de catalizadores de níquel[2].

En este trabajo se presenta una primera aproximación a la síntesis de viniliden-ciclopentanos mediante secuencias de ciclación/acoplamiento radicálico catalizadas por níquel a partir de 8-bromo-1,6-eninos y bromuros de organozinc. En el estudio metodológico desarrollado, se ha evaluado el papel desempeñado por diferentes ligandos nitrogenados bi- y tridentados así como la naturaleza de los bromuros de organozinc alquílicos y arílicos empleados. Hasta el momento, en las condiciones ensayadas para la reacción con bromuros de **alquil**zinc se han obtenido únicamente los productos de acoplamiento alénico no ciclados, mientras que los ensayos realizados con bromuro de **fenil**zinc han proporcionado el aleno de cadena abierta acompañado del correspondiente vinilidenciclopentano como producto minoritario de la reacción (*Esquema 1*).



Esquema 1

[1] Hoffmann-Röder, A.; Krause, N. *Angew. Chem. Int.* **2004**, *43*, 1196.

[2] Soler-Yanes, R.; Arribas-Álvarez, I.; Guisán-Ceinos, M.; Buñuel, E.; Cárdenas, D. J. *Chem. Commun.* **2017**, *23*, 1584.

New antagonists of LPA_1 and LPA_2 lysophosphatidic acid receptors

A. Andrea Escobar Peña

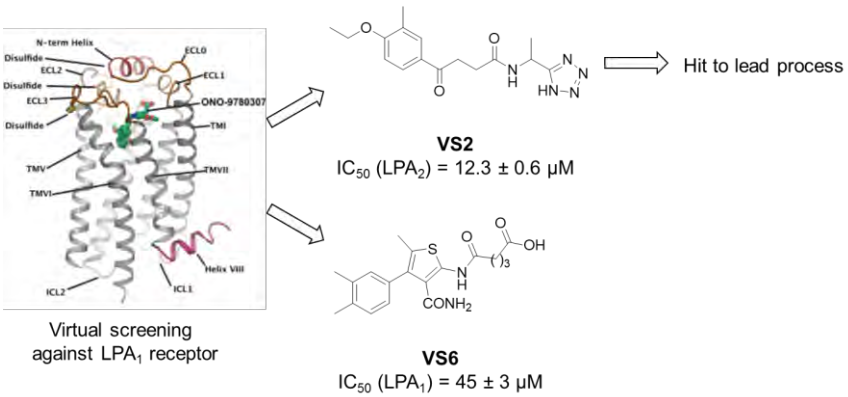
Dpto de Química Orgánica I, Facultad de Ciencias Químicas, Universidad Complutense de Madrid, E-28040 Madrid, Spain

e-mail: anaescob@ucm.es

***Keywords**: lysophosphatidic acid, LPA_1 receptor, LPA_2 receptor, LPA receptor antagonists*

G protein-coupled receptors (GPCRs) are important therapeutic targets given that almost half of the drugs in the market act on some type of GPCR. Within these receptors stand out those whose endogenous ligands are lipid molecules and, in particular, lysophosphatidic acid (LPA),[1] a molecule that elicits a plethora of biological effects by binding to specific GPCRs (LPA_1-LPA_6).[2] Among these receptors, LPA_1 and LPA_2 deserve special attention since they are involved in many pathologies that affect to the central nervous system[3] as well as in cancer.[4] However, no potent and selective antagonists for these receptors have been described so far.

In this context, in our group, we have started a project focused on the development of new selective and potent antagonists for LPA_1 and LPA_2 receptors. Towards this aim, we have performed a virtual screening of ZINC database against the LPA_1 receptor and we have identified two hits, VS2 and VS6, with activity at the LPA_2 and LPA_1 receptors respectively. Then, we have set up synthetic routes that allow access to these two hits as well as derivatives to perform subsequent structure-activity relationship studies. The ongoing hit to lead process, including the selectivity profiles against the rest of LPA receptors will be studied. These new compounds will constitute a set of tools well-suited to aid the elucidation of the (physio)pathological roles of individual LPA receptors.



References: [1] Mutoh, T.; Rivera, R.; Chun, J. *Br. J. Pharmacol.* **2012**, *165*, 829. [2] González-Gil, I.; Zian, D.; Vázquez-Villa, H.; Ortega-Gutiérrez, S.; López-Rodríguez, M.L. *Med. Chem. Commun.* **2015**, *6*, 13. [3] Velasco, M.; O'Sullivan, C.; Sheridan, G.K. *Neuropharmacology* **2017**, *113*, 608. [4] Yunzho, D.; Yong, W.; Mei-Zhen, C.; Xuemin, X. *Mediat. Inflamm.* **2017**, DOI: 10.1155/2017/2754756.

Carbohydrate influence on the interaction of glyco-Hoechst derivatives with DNA minor groove of A_2T_2 and A_3T_3 oligonucleotides sequences.

Figuerola, A.; García-Puentes, D.; Taladriz-Sender, A.; Vicent, C*.

Instituto de Química Orgánica General, CSIC, Juan de la Cierva 3, 28006, Madrid, Spain.
e-mail: cvicent@iqog.csic.es

***Keywords**: DNA interaction, carbohydrate, hydrogen bonding.*

The objective of this general project is to quantify the carbohydrate interaction with the DNA minor groove. This study is relevant since carbohydrates are present in antibiotic and anticancer drugs that interact with DNA. In addition, there are some glycoproteins like transcription factors where the sugar is involved in the interaction with the DNA.[1]

The strategy of this project is to design a vector that is able to carry the carbohydrate into the DNA minor groove.[2] In this work we have chosen a Hoechst derivative[3] as a vector (Fig. 1). The sugar is joined to the vector by an amide group in the carbohydrate anomeric position.[4]

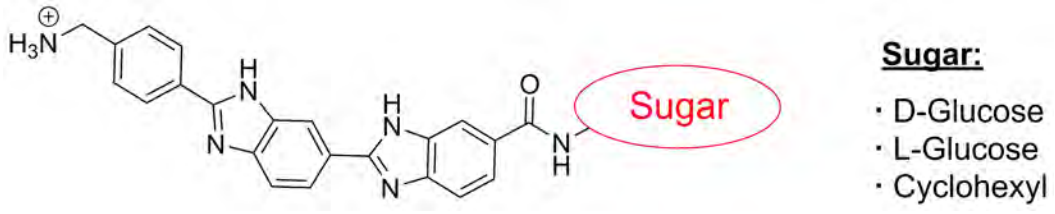


Figure 1. Glyco-Hoechst derivates structures.

We are going to present their design, synthesis and interaction studies with oligonucleotides containing A_2T_2 and A_3T_3 sequences by circular dichroism.

The carbohydrate contribution to the binding will be evaluated and effects of the sugar chirality will be shown by comparing D-Glucose-Hoechst and L-Glucose-Hoechst derivates.

References:
[1] Tang, C.; Paul, A.; Alam, M. P.; Roy, B.; Wilson, W. D.; Hecht, S. M., J. Am. Chem. Soc. **2014**, 136, 13715-13726. [2] Blázquez-Sánchez, M.T.; Marcelo, F.; Fernández-Alonso, M.C.; Poveda, A.; Jiménez-Barbero, J.; Vicent, C., Chem. Eur. J. **2014**, 20, 17640-17652. [3] (a) Behrens, C.; Harrit, N.; Nielsen, P. E. *Bioconjugate Chemistry* **2001**, *12*, 1021–1027. (b) Bunkenborg, J.; Behrens, C.; Jacobsen, J., Bioconjugate Chem. **2002**, 13, 927-936. [4] Doctoral Thesis Diego García-Puentes, in progess.

SÍNTESIS DE SULFÓXIDOS MEDIANTE UNA REACCIÓN TÁNDEM TIOL-ENO/OXIDACIÓN FOTOCATALIZADA

A.M. Martínez Gualda, E. Ming, A. Guerrero, A. Fraile, J. Alemán

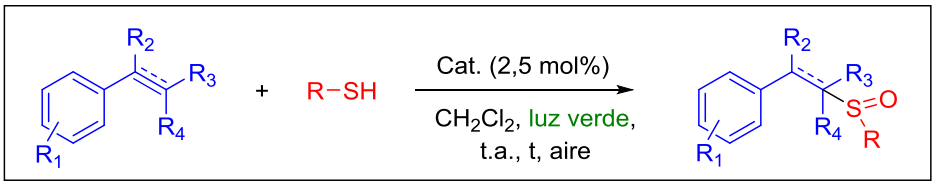
Departamento de Química Orgánica, Universidad Autónoma de Madrid, 28049 Madrid, España
anamaria.martinezg01@estudiante.uam.es

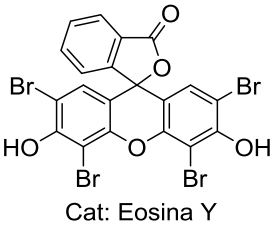
***Keywords**: fotocatálisis, oxidación, sulfóxidos*

El grupo sulfinilo tiene una importancia relevante en química orgánica: como auxiliar quiral en síntesis asimétrica, como reactivo en la reacción de Pummerer y Mislow-Evans para la obtención de α-acil-tioéteres y alcoholes alílicos, respectivamente, o a modo de agente terapeútico actuando como inhibidor de la bomba de protones.[1] Es por ello que, desde que Märcker describió en 1865 la primera síntesis de sulfóxidos, se hayan desarrollado muchos métodos para la formación de éstos.[2] Sin embargo, la mayoría de ellos implican el uso de peróxidos o perácidos, los cuales conllevan riesgos asociados además de la obtención de las correspondiente sulfonas debido a la sobreoxidación.[3]

Recientemente, nuestro grupo de investigación ha descrito la síntesis de una gran variedad de sulfóxidos a partir de tioéteres empleando un complejo de Platino (II), oxígeno atmosférico y luz.[3] Por otro lado, es conocido que la reacción fotocatalizada tiol-eno permite la formación de tioéteres de una forma eficiente.[4] Por tanto, nos preguntamos si sería posible la obtención de sulfóxidos en un proceso tándem de reacción tiol-eno y oxidación.

En esta comunicación presentamos la primera síntesis fotoorganocatalizada tándem tiol-eno/oxidación de sulfóxidos a partir de tioles y alquenos o alquinos. El uso de un foto-organocatalizador como la Eosina Y (evitando de este modo la presencia de metales), la luz como fuente de energía y el oxígeno presente en el aire como agente oxidante, convierte nuestra metodología en una alternativa atractiva y medioambientalmente sostenible para la síntesis de sulfóxidos a partir de dobles y triples enlaces.





Cat: Eosina Y

References:

[1] Zhang, Y.; Wong, Z. R.; Wu, X.; Lauw, S. J. L.; Huang, X.; Webster, R. D.; Chi, Y. R. *Chem. Commun.* **2017,** *53*, 184.

[2] Kowalski, P.; Mitka, K.; Ossowska, K.; Kolarska, Z. *Tetrahedron* **2005,** *61*, 1933.

[3] Casado-Sanchez, A.; Gomez-Ballesteros, R.; Tato, F.; Soriano, F. J.; Pascual-Coca, G.; Cabrera, S.; Aleman, J. *Chem. Commun.* **2016,** *52*, 9137.

[4] Tyson, E. L.; Ament, M. S.; Yoon, T. P. *J. Org. Chem.* **2013,** *78*, 2046.

Molecular engineer for the design and synthesis of new charge transporting materials in perovskites solar cells

P.D. García Fernández,[a] J.Urieta Mora,[a] A.Molina Ontoria,[a] N. Martín León [a, b]

[a] *IMDEA-Nanoscience, C/Faraday, 9, Ciudad Universitaria de Cantoblanco, 28049, Madrid, Spain*

[b] *Departamento de Química Orgánica I, Facultad de Ciencias Químicas, Universidad Complutense, 28040, Spain*

e-mail: pedrga02@ucm.es

***Keywords**: Perovskite solar cells, power conversion efficiencies, hole transporting materials.*

Photovoltaics has become a convenient method for light to energy conversion in a clean and infinitely renewable manner. [1] In this field, perovskite solar cells (PSCs) are an emerging technology that exhibits excellent power conversion efficiencies (PCEs).[2] PSCs photovoltaic performance is highly improved by the integration of charge selective contact, such as hole transporting materials (HTMs) and/or electron transporting materials (ETMs).[3]
In this work, three new molecules have been synthesized through facile synthetic routes. Electrochemical characterization of compounds **2a** and **2b** reveal an estimated HOMO energy similar to that of the benchmark HTM, Spiro-OMeTAD, [4] which ensure an efficient hole injection to the mixed-ion perovskite material $(FAPbI_3)_{0.85}(MAPbBr_3)$. On the other hand, compound **1** exhibits much deeper HOMO energy (-5.8 eV), which makes it suitable as promising HTM for wide-bandgap perovskite $MAPbBr_3$.

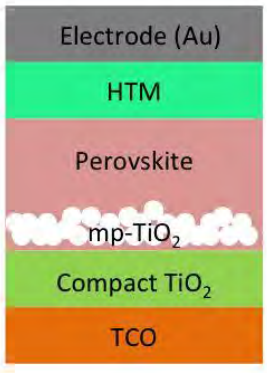


Figure 1. PSC general architecture.

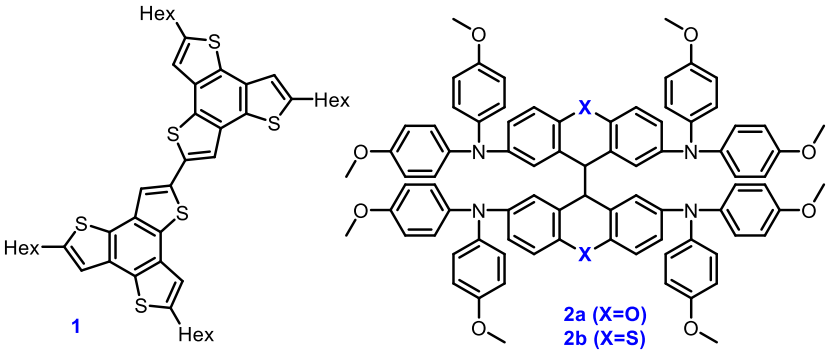


Figure 2. Molecules synthesized and used as HTMs.

References:

[1] Polman, a.; Knight, M.; Garnett, E. C.; Ehrler, B.; Sinke, W. C. *Science*, **2016**, *352*, 307.
[2] (a) Meng, L.; You, J.; Guo T. F.; Yang, Y. *Acc. Chem. Res.* **2016**, *49*, 155. (b) Grätzel, M. *Nature Materials*, **2014**, *13*, 838.
[3] Calió, L.; KAzim, S.; Grätzel, M.; Ahmad, S. Angew. *Chem. Int. Ed*. **2016**, *55*, 2.
[4] Saliba, M.; Matsui, T.; Seo, J-Y.; Domanski, K.; Correa-Baena, J-P.; Nazeeruddin, M. K.; Zakeeruddin, S. M.; Tress, W.; Abate, A.; Hagfeldt, A.; Graetzel, M. *Energy Environ. Sci.,* **2016,** *9*, 1989.

Copper-catalyzed synthesis of cyclic phosphonates

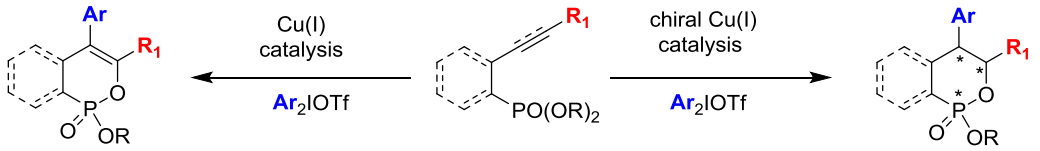
N. Vázquez-Galiñanes, B. Pérez-Saavedra, C. Saá, M. Fañanás-Mastral

Centro Singular de Investigación en Química Biolóxica e Materiais Moleculares (CIQUS) e Departamento de Química Orgánica, Universidade de Santiago de Compostela, 15782, Santiago de Compostela
nuria.vazquez.galinanes@rai.usc.es

Keywords: *Copper catalysis, phosphonates, diaryliodonium salts.*

Cyclic organic phosphonates represent a highly important class of compounds with a wide range of applications in organic synthesis and medicinal chemistry. Some of them are enzyme inhibitors or present antitumor activity.[1] Several methodologies to synthesize these compounds have been developed.[2] However, they are associated to selectivity problems and they usually involve the use of stoichiometric amounts of metal complex or halogenated reagents. Given the importance of these compounds, the development of new catalytic methods for their synthesis is highly desirable.

Diaryliodonium salts which are air stable, non-toxic and easy to prepare compounds, have recently gained considerable attention as selective arylating reagents in organic synthesis.[3] These hypervalent iodine compounds react with Cu(I) complexes to afford highly electrophillic aryl-Cu(III) intermediates.[4] This strategy has been applied to the arylation of a range of unsaturated substrates.[5]



Cyclic enol phosphonates **Cyclic dialkyl phosphonates**

In this work a catalytic methodology based on the use of diaryliodonium salts as arylating agents and CuCl as catalyst has been developed. It is proposed that the cyclic phosphorous compounds are formed through a tandem process in which aryl-Cu(III) species, catalytically generated by reaction between the diaryliodonium salt and the Cu(I) catalyst, reacts with an alkynyl phosphonate affording a vinyl cation intermediate which is trapped by the oxygen atom of the phosphoryl group by an intramolecular nucleophilic addition. This novel catalytic protocol features a chemoselective arylation of the alkyne versus the phosphoryl group. In addition, the reaction of alkenyl phosphonates with diaryliodonium salts wich afford cyclic dialkyl phosphonates bearing three different stereocenters has been studied.

References:

[1] (a) Li, B.; Zhou, B.; Lu, H.; Ma, L.; Peng, A.-Y. *Eur. J. Med. Chem.***2010**, *45*, 1955-1963. (b) Kaur, K.; Lan, M. J. k.; Pratt, R. F. *J. Am. Chem. Soc.* **2001**, *123*, 10436-10443.
[2] (a) Peng, A.; Hao, H.; Li, B.; Wang, Z.; Du, Y. *J. Org. Chem.* **2008**, *73*, 9012-9015. (b) Seo, J.; Park, Y.; Jeon, I.; Ryu, T.; Park, S.; Lee, *P. Org. Lett*. **2013** , *15*, 3358-3361.
[3] Merrit, E. A.; Olofsson, B. Angew. *Chem. Int.* Ed. **2009**, *48*, 9052-9070
[4] (a) Hickman, A. J.; Sanford, M. S. *Nature* **2012**, *484*, 177−185. (d) Casitas, A.; Ribas, X. *Chem. Sci*. **2013**, *4*, 2301−2318.
[5] Fañanás-Mastral, M. *Synthesis* **2017**, *49*, 1905-1930.

Synthesis of molecules inspired on microbiota metabolites and phenotypic study in cancer stem cells

Paloma P. Mayo Mariscal de Gante, Sergio Algar Lizana, Henar Vázquez Villa, Bellinda Benhamú Salama, Mª Luz López Rodríguez

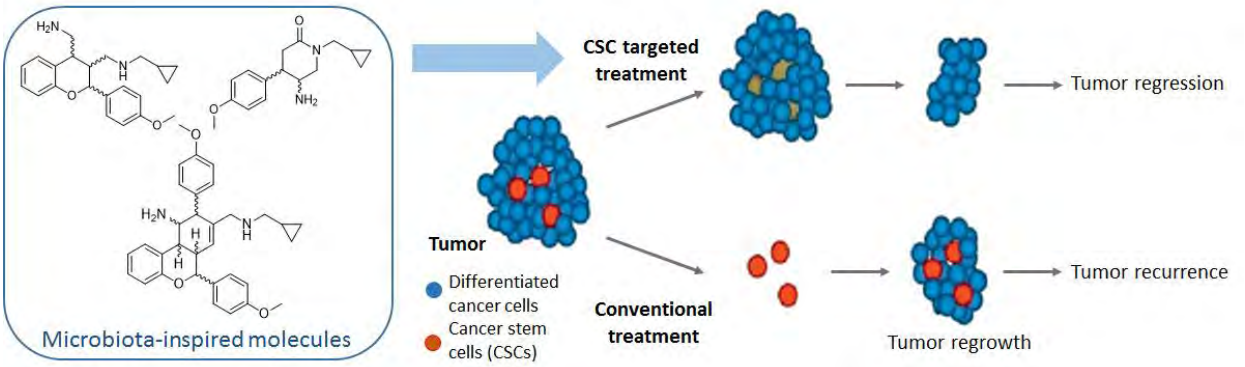
Dpto. de Química Orgánica I, Fac. de CC. Químicas, Universidad Complutense de Madrid, E-28040, Madrid, Spain
e-mail: pmayo@ucm.es

***Keywords**: microbiota metabolites, cancer stem cells*

In recent years, several diseases have been linked to alterations of the human microbiome, including cancer,[1] diabetes[2] and immune system dysfunction.[3] These findings support the hypothesis that metabolites produced by the microbiota could represent an unexplored chemical space endowed with interesting biological activities.[4] In this context, our research group initiated a project aimed at the development of new molecules inspired on microbiota metabolites that could lead to novel therapeutic strategies. In particular, the present work is focused on the identification of new compounds able to regulate the differentiation process of cancer stem cells (CSCs), due to their key role in tumor initiation, progression and recurrence.

Toward this aim, we have designed a set of structurally diverse compounds bearing previously identified microbiota metabolites. Herein, we describe the synthesis of six new molecules that contain three different scaffolds, obtained in a straightforward and stereocontrolled manner using multicomponent organocatalytic reactions.

Synthesized compounds are currently under evaluation to determine their capacity to induce CSCs differentiation and/or selective death, which could offer a novel approach for cancer treatment.



References: [1] (a) Perez-Chanona, E. *et al. Curr. Opin. Immunol.* **2016**, *39*, 75. (b) Schwabe, R.F. *et al. Nat. Rev. Cancer* **2013**, *13*, 800. [2] (a) Bouter, K.E. *et al. Gastroenterology* **2017**, *152*, 1671. (b) Qin, J. *et al. Nature* **2012**, *490*, 55. [3] Levy, M. *et al. Curr. Opin. Microbiol.* **2017**, *35*, 8. [4] Mimee, M. *et al. Adv. Drug Deliv. Rev.* **2016**, *105*, 44.

Synthesis and Purification of Oligonucleotides

Saúl Rubio González, María Dolores Company Mateos

Sylentis S.A.
Saul.rubiog@estudiante.uam.es

***Keywords**: (Interfering RNA, purification, oligonucleotides)*

The objective of this Master`s Project is to obtain an oligonucleotide of 19 units, as well as to carry out the development of methods of purification and characterization of the main impurities of the same. The design and synthesis have been set up by the laboratory, whose mechanism is based on the RNA interference process (RNAi). RNAi produces gene silencing specifically through the use of small double-stranded RNA molecules called small interfering RNA (siRNA), in our case of 19 nucleotides each. Its production consists of a series of chain reactions, in which the different reactive centers of the molecule are protected and unprotected cyclically. The procedure consisted in preparing the strands separately by a solid phase synthesis and then the corresponding hybridization of both obtaining the desired RNA duplex.

Finally, the main chromatographic techniques for the study of impurities from both chains, sense and antisense, have been ion exchange and size exclusion high performance liquid chromatography.

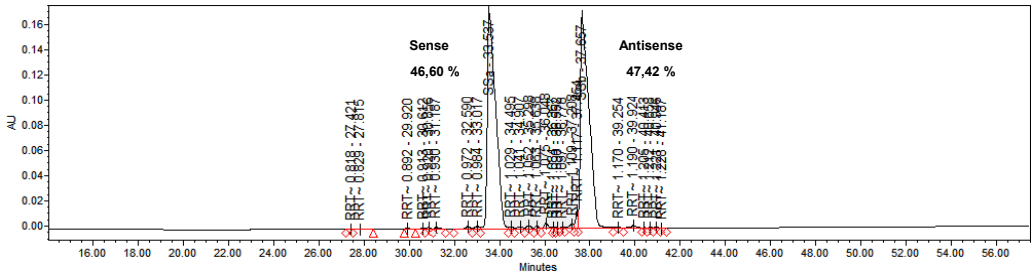


Figure 1. Duplex by HPLC-IEX denaturing method

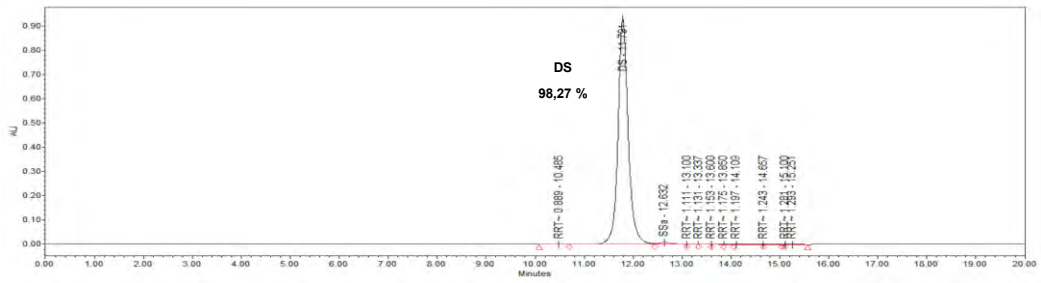


Figure 2. Duplex by HPLC-SEC non denaturing method

[1] Okafo, G; Elder, D; Webb, M. *Analysis of oligonucleotides and their related substances*; ILM Publications: Hertfordshire, UK, 2013.

[2] Bonilla, J; Srivatsa, G. *Handbook of Analysis of Oligonucleotides and Related Products*; CRC Press: Boca Raton, FL, 2011.

Desarrollo y estudio de modelos de membrana protocelular basados en nuevos nucleolípidos y su capacidad para formar micelas y vesículas con propiedades biológicas.

I. de la Torre Jarrín, S. Morales Reina, A. de la Escosura Navazo

Departamento de Química Orgánica, Universidad Autónoma de Madrid, Cantoblanco, 28049 Madrid
e-mail: isabel.torre@estudiante.uam.es; sara.morales@uam.es; andres.delaescosura@uam.es

***Keywords**: nucleolípidos, bases nitrogenadas.*

Los nucleolípidos constituyen uno de los objetos de estudio de la química de sistemas.[1-4] Su aplicación tiene un gran futuro en áreas como la ciencia de materiales y la biomedicina, ya que combinan las propiedades de los lípidos para autoensamblarse y la complementariedad entre bases que presentan las bases nitrogenadas.[5] En este proyecto, se han sintetizado cinco derivados de ácido (S)-2,3-diaminopropiónico (DAP), que son portadores de timina (T), adenina (Ad) o de ambas bases. En dos de estos derivados, el grupo ácido carboxílico de este aminoácido no natural se ha funcionalizado con alcohol oleico para formar un éster. En los otros tres compuestos sintetizados, el grupo carboxílico se ha transformado en un tioéster cuyo grupo saliente (tiol) permitiría en un principio que se dé la transtioesterificación con tiol oleico. Todos estos acoplamientos se llevan a cabo utilizando carbodiimidas y aditivos típicos en la metodología de la formación de enlaces amida. Después de la síntesis, se están llevando a cabo experimentos de autoensamblaje sobre plantillas de ADN y el siguiente objetivo es la realización de experimentos de autocatálisis (Figura 1).

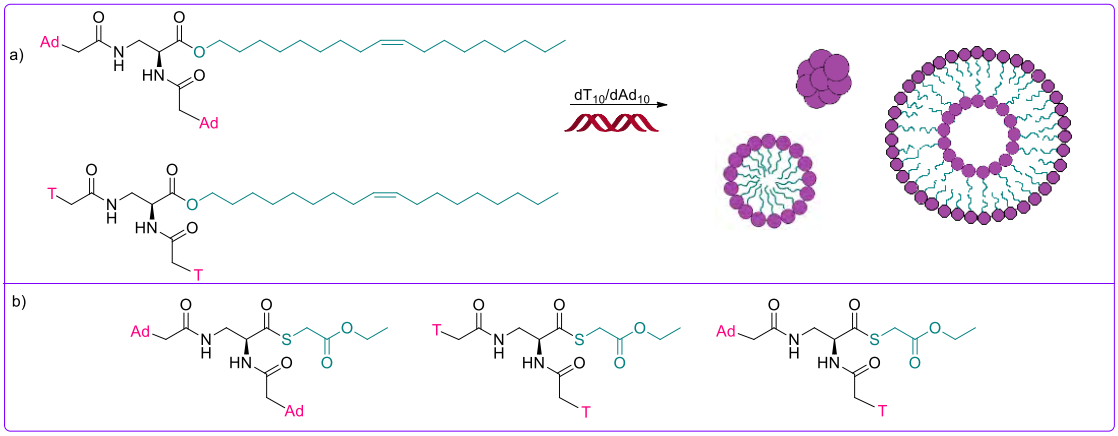


***Figura 1.** a) Experimentos de autoensamblaje sobre plantillas de ADN. b)Futuros experimentos de autocatálisis física.*

References:

[1] Giuseppone N. *Acc. Chem. Res.* 2012, *45*, 2178. [2] Mattia E.; Otto S. *Nat. Nanotech.* 2015, *10*, 111. [3] Ruiz-Mirazo K.; Briones C.; de la Escosura A. *Chem. Rev.* 2014, *114*, 285. [4] Ruiz-Mirazo K.; Briones C.; de la Escosura A. *Open Biol.* 2017, *7*, 170050. [5] Rosemeyer H. *Chem. & Biodiversity*, 2005, *2*, 977.

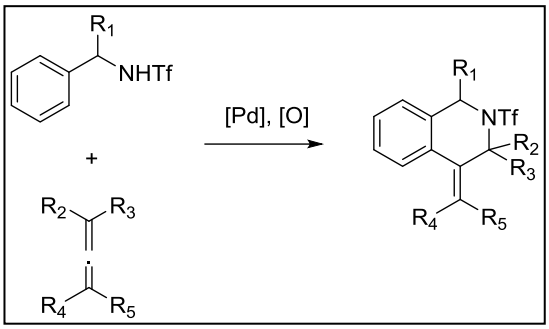
C-H functionalization of benzylamines with allenes and their application in tropane synthesis

Xandro Vidal, José Luis Mascareñas[a], and Moisés Gulías[a]

[a] *Centro Singular de Investigación en Química Biolóxica e Materiais Moleculares (CiQUS) and Departamento de Química Orgánica, Universidad de Santiago de Compostela, 15782 Santiago de Compostela, Spain*
xandrovp@gmail.com

***Keywords**: C-H activation, palladium, benzylamine*

During the past years our group has been studying novel C-H functionalization with alkynes and allenes catalysed by Rh(III) and Pd(III).[1] In this communication, we present a palladium catalyzed C-H activation of benzylamines and their subsequent coupling with allenes. This constitutes an interesting method in the synthesis of heterocyclic natural products. This type of reaction has been reported previously only in a limited way.[2] In their case, their method needs electron withdrawing groups in the α position of the amine, and only tolerates primary allenes. We developed a novel reaction between benzylamines and allenes that overcomes these limitations. Herein we also show how we developed this reaction and how we applied it in the synthesis of tropanes using intramolecular catalysis.



References:

[1] (a) Seoane, A.; Casanova, N.; Quiñones, N.; Mascareñas, J. L.; Gulías, M. *J. Am. Chem. Soc.* **2014**, *136*, 7607. (b) Seoane, A.; Casanova, N.; Quiñones, N.; Mascareñas, J. L.; Gulías, M. *J. Am. Chem. Soc.* **2014**, *136*, 834. (c) Casanova, N.; Del Rio, K. P.; García-Fandiño, R.; Mascareñas, J. L.; Gulías, M. *ACS Catal.* **2016**, *6*, 3349. (d) Casanova, N.; Seoane, A.; Mascareñas, J. L.; Gulías, M. *Angew. Chem., Int. Ed.* **2015**, *54*, 2374

[2[Rodríguez, A.; Albert, J.; Ariza, X.; Garcia, J.; Granell, J.; Farràs, J.; La Mela, A.; Nicolás, E. *J. Org. Chem.* **2014**, *79* , 9578.

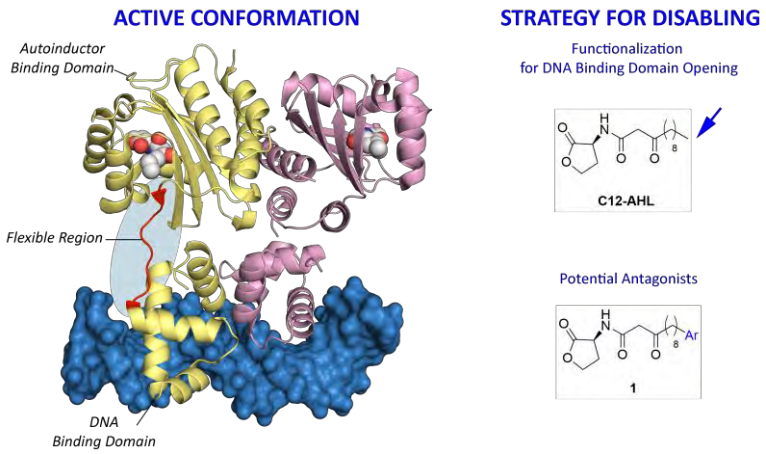
Disabling *Pseudomonas aeruginosa* Virulence by Causing Conformational Changes in the Quorum Sensing Modulator LasR

Ángela Rodríguez Costa and Concepción González Bello*

Centro Singular de Investigación en Química Biolóxica e Materiais Moleculares (CIQUS) and Departamento de Química Orgánica, Universidade de Santiago de Compostela, Jenaro de la Fuente s/n, 15782 Santiago de Compostela, Spain. *E-mail: concepcion.gonzalez.bello@usc.es

Keywords: *bacterial virulence*, *hospital-acquired infections, antagonists*

In recent years a new strategy for the treatment of infectious diseases is currently been explored as an alternative strategy to the treatment with antibiotics that destroy its viability. It involves the inactivation of the *bacterial capacity to produce the infection*, i.e. its pathogenicity.[1] The attenuation of bacterial virulence will make the bacterium less able to establish successful infection and, in consequence, it would be cleared by the host immune response or the antibiotic. Besides anti-virulence drugs have not yet reached clinical trials, it is however a promising strategy since these compounds would create an *in vivo* scenario similar to that achieved by vaccination with a live attenuated strain. In this project, we address the development of new anti-virulence agents by deactivating LasR, a transcriptional quorum modulator in *Pseudomonas aeruginosa,*[2] which causes about 13% of severe healthcare-associated infections that are multidrug resistant to nearly all antibiotics. Our strategy consists in the formation of LasR/ligand complexes of inappropriate conformation to trigger its dimerization[3] and subsequent activation of the virulence process. To this end, we have synthesized several analogs of the natural autoinducer *N*-(3-oxododecanoyl)-L-homoserine lactone (C12-AHL) as potential antagonist of LasR.



[1] Garland, M.; Loscher, S.; Bogyo, M. *Chem. Rev*. **2017**, *117*, 4422.
[2] http://www.who.int/mediacentre/news/releases/2017/bacteria-antibiotics-needed/es/
[3] Tan, S. Y.-Y.; Chua, S.-L.; Chen, Y.; Rice, S. A.; Kjelleberg, S.; Nielsen, T. E.; Yang, L.; Givskov, M. *Antimicrob. Agents Chemother*. **2013**, *57*, 5629.

Development of antibody-drug conjugates as antituberculosis drugs

Luke Anthony Spear, Mar Martín-Fontecha, María Luz López Rodríguez

Dpt. de Química Orgánica I, Fac. de CC. Químicas, Universidad Complutense de Madrid, E-28040, Madrid, Spain
e-mail: lspear@ucm.es

***Keywords**: tuberculosis, drug delivery, antibody-antibiotic conjugate*

Tuberculosis (TB) is the leading infectious cause of death worldwide, with 1.4 million deaths reported in 2016.[1] The treatment of this disease involves a lengthy regime, particularly when multidrug resistant-TB strains are the infectious agent to treat (up to 24 months of therapy with four to six drugs). Accordingly, more efficacious treatments are clearly needed. One of the main weaknesses of the current drugs is that many of them do not reach the granuloma, the site where the bacteria reside, fact that limits their efficacy.[2] These findings suggest that targeted drug delivery could help improving clinical success by selectively eliminating these bacterial niches. In this regard, the recent success on the treatment of intracellular *S. aureus* using site-specific antibody-drug conjugates[3] suggests that this approach may be promising for the treatment of *M. tuberculosis*.

In light of these results, the aim of this project is the development of antibody-antibiotic conjugates for the treatment of tuberculosis by attachment of first-line antibiotics, such as isoniazid, to monoclonal antibodies (mAb) that recognize *M. tuberculosis*. Both moieties are bound by an enzymatically cleavable linker (Figure 1).

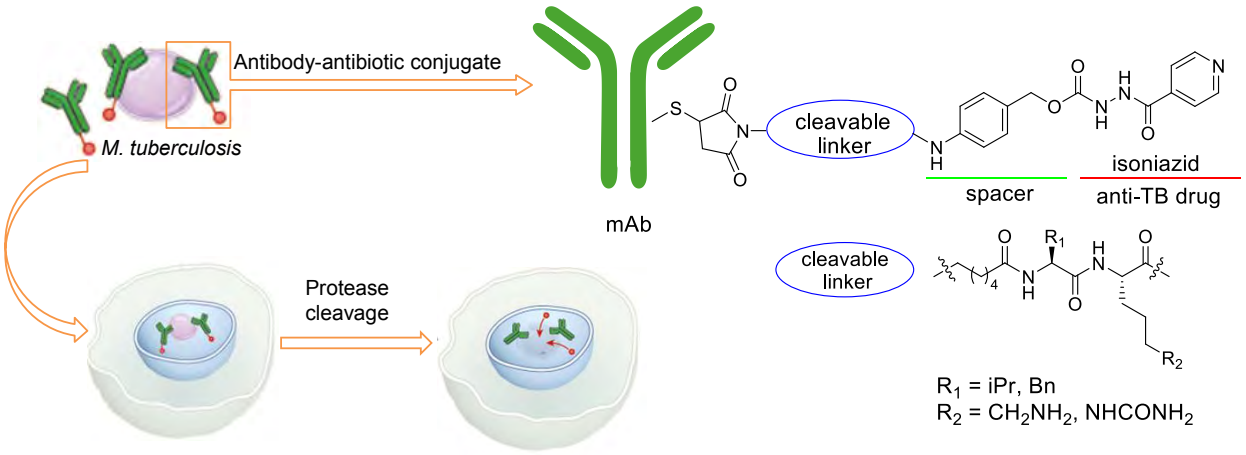


Figure 1. Representative antibody-antibiotic conjugates.

References:

[1] Global Tuberculosis Report 2016. World Health Organization 2016. http://apps.who.int/medicinedocs/es/d/Js23098en/

[2] Dartois, V. *Nat. Rev. Microbiol.* **2014**, *12*, 159.

[3] (a) Lehar, S.M. *et al. Nature* **2015**, *527*, 323; (b) Mariathasan, S. *et al. Trends Mol. Med.* **2017**, *23*, 135.

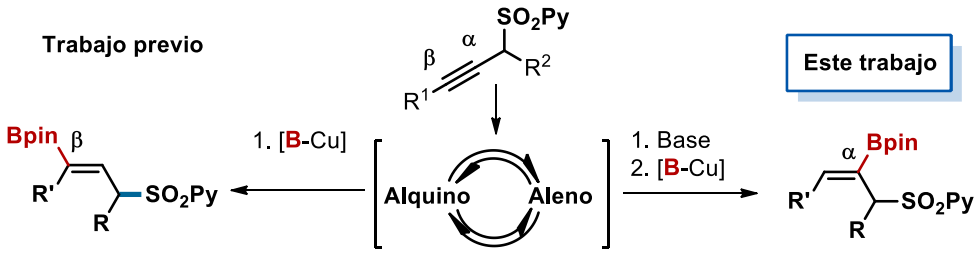
REACCIONES DE BORILACIÓN DE PROPARGIL 2-PIRIDILSULFONAS: PROCESOS DE INVERSIÓN DE LA REGIOQUÍMICA HABITUAL

C. Maquilón, A. G. Rubia, S.-H. Kim, P. Mauleón,* R. Gómez Arrayás,* J. C. Carretero*

[1] Universidad Autónoma de Madrid, Departamento de Química Orgánica, Facultad de Ciencias, Cantoblanco, 28049 Madrid, Spain. cristina.maquilon@estudiante.uam.es

Palabras clave: Regioselectividad, borilación, alquinos, efecto del ligando

Los vinil boronatos son intermedios sintéticos estratégicos en la preparación de alquenos altamente sustituidos. Sin embargo, los métodos de síntesis tradicionales de vinil boronatos a partir de alquinos internos requieren condiciones de reacción severas, y además habitualmente transcurren con una pobre regioselectividad. Métodos recientes para su preparación que implican el uso de especies de boro nucleófilas de tipo boril-cobre suponen una alternativa a la hidroboración tradicional que permite el acceso a alquenil boronatos a partir de alquinos asimétricos con elevada regioselectividad y tolerancia funcional. En particular, una serie de trabajos recientes han descrito el acceso a la mayoría de los patrones de sustitución dentro del marco de las hidrosililaciones e hidroboraciones de alquinos terminales e internoas. Este trabajo se centra en la exploración de reacciones de α-borilación de alquinos internos asimétricamente sustituidos que contengan en posición propargílica el grupo (2-piridil)sulfonilo empleando un sistema catalítico cobre(I)/diboro. Para obtener este patrón de sustitución, el único no descrito hasta el momento,[1] se describe una estrategia que combina la influencia de los ligandos empleados en la formación del complejo boril-cobre y el efecto de distintas bases capaces de promover una isomerización alquino-aleno, modificando la reactividad del proceso hacia la síntesis del regioisómero α-borilado.



Referencias

[1] a) A. L. Moure, R. Gómez Arrayás, D. J. Cárdenas, I. Alonso, J. C. Carretero. *J. Am. Chem. Soc.* **2012**, *134*, 7219–7222. b) A. L. Moure, P. Mauleón, R. Gómez Arrayás, J. C. Carretero. *Org. Lett.* **2013**, *15*, 2054–2057.

3-Ariltriazolopirimidinas frente a la replicación del virus chikungunya: estrategias de síntesis

Oscar Orozco y M. J. Pérez-Pérez

Instituto de Química Médica (IQM-CSIC), Juan de la Cierva 3, 28006 Madrid

e-mail: osorozco@ucm.es

***Keywords**: triazolopirimidinas, virus Chikungunya, enfermedades emergentes*

La fiebre de chikungunya (CHIKF) es una enfermedad arboviral causada por el virus chikungunya (CHIKV), cuyo vector principal son los mosquitos del género *Aedes*. La expansión de estos mosquitos a zonas templadas, particularmente el *Aedes albopictus*, ha contribuido significativamente a la expansión de la fiebre chikungunya que se considera actualmente una enfermedad global emergente.[1] El virus chikungunya CHIKV ataca a los fibroblastos, afectando a los músculos, las articulaciones y los tejidos conectivos provocando mialgia y artralgia. Es una enfermedad incapacitante con importes consecuencias económicas y sociales. No existe tratamiento específico ni vacuna comercialmente disponible para prevenir la infección por este virus. Por tanto es urgente la búsqueda de compuestos capaces de inhibir la replicación de CHIKV.[2]

En nuestro grupo de investigación hemos descrito una serie de 3-aril [1,2,3]triazolo[4,5-*d*]pirimidin-7(6*H*)-onas,[3] que inhiben de modo selectivo la replicación del CHIKV. Para la obtención de estos compuestos se han seguido dos rutas sintéticas diferentes que permiten la incorporación de distintos sustituyentes tanto en el anillo de triazolopirimidina como en el resto de arilo. Además se ha utilizado un derivado fenólico protegido para la incorporación de distintos sustituyentes sobre la posición 3 del arilo.

Agradecimientos: Este proyecto está financiado por MINECO/FEDER (SAF2015-64629-C2-1-R)

1. Rougeron, V.; Sam, I. C.; Caron, M.; Nkoghe, D.; Leroy, E.; Roques, P. Chikungunya, a paradigm of neglected tropical disease that emerged to be a new health global risk. *J. Clin. Virol.* **2015,** *64*, 144-152.

2. Abdelnabi, R.; Neyts, J.; Delang, L. Chikungunya virus infections: time to act, time to treat. *Curr. Opin. Virol.* **2017,** *24*, 25-30.

3. Gigante, A.; Canela, M. D.; Delang, L.; Priego, E. M.; Camarasa, M. J.; Querat, G.; Neyts, J.; Leyssen, P.; Pérez-Pérez, M. J. Identification of 1,2,3 Triazolo 4,5-d pyrimidin-7(6H)-ones as Novel Inhibitors of Chikungunya Virus Replication. *J. Med. Chem.* **2014,** *57*, 4000-4008.

Micelas a Partir de Copolímeros PEG-Dendrímero Funcionalizados

X. Lago, J. Correa, S. Parcero, R. Riguera, E. Fernández-Megía*.

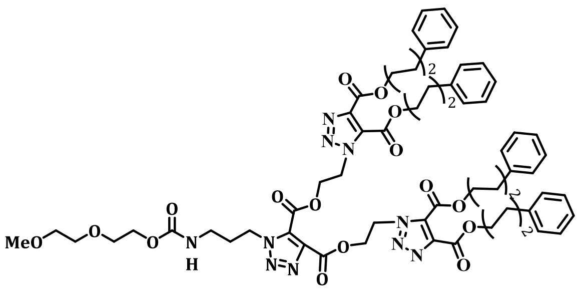
CiQUS – Universidade de Santiago de Compostela

xade.lago@rai.usc.es

***Palabras clave**: dendrímeros, copolímeros, micelas.*

Las micelas anfipáticas son nanopartículas esféricas que tienden a formarse en medio acuoso a causa de interacciones entre las moléculas que las forman [1]. Los copolímeros PEG-dendrímero están formados por una cadena de polietilenglicol y un dendrímero [3], formando una estructura anfifílica. Representan una potencial vía de transporte de fármacos, especialmente por su parte PEGilada, ya que este polímero presenta una mínima activación del sistema inmunitario en el organismo[2].

En este trabajo se sintetizaron copolímeros PEG-dendrímero a partir de PEG5000 y un bloque dendrítico que se hizo crecer partiendo de un punto focal unido a la cadena lineal [4]. También se sintetizó una unidad de repetición de crecimiento y otra de funcionalización. Con esta última se obtuvieron los productos PEG-[G2]-Ar y PEG-[G4]-Ar, con los que se formaron micelas de 16 y 38 nm respectivamente.



Referencias:

[1] Newkome, G.R.; Yao, Z.; Baker, G. R.; Gupta, V. K., *Journal of Organic Chemistry*, **1985**, *50*, 2003-2004.

[2] Tomalia, D.A.; Baker, H.; Dewald, J.; Hall, M.; Kallos, G.; Martin, S.; Roeck, J.; Ryder, J.; Smith, P., *Polymer Journal*, **1985**, *17*, 117-132.

[3] Alcantar, N. A.; Aydil, E. S; Israelachvili, J. N., *Journal of Biomedical Materials Research*, **2000**, *51*, 343-351.

[4] Sousa-Herves, A.; Novoa-Carballal, R.; Riguera, R.; Fernández-Megía, E., *APPS Journal*, **2014**, *16*, 948-961.

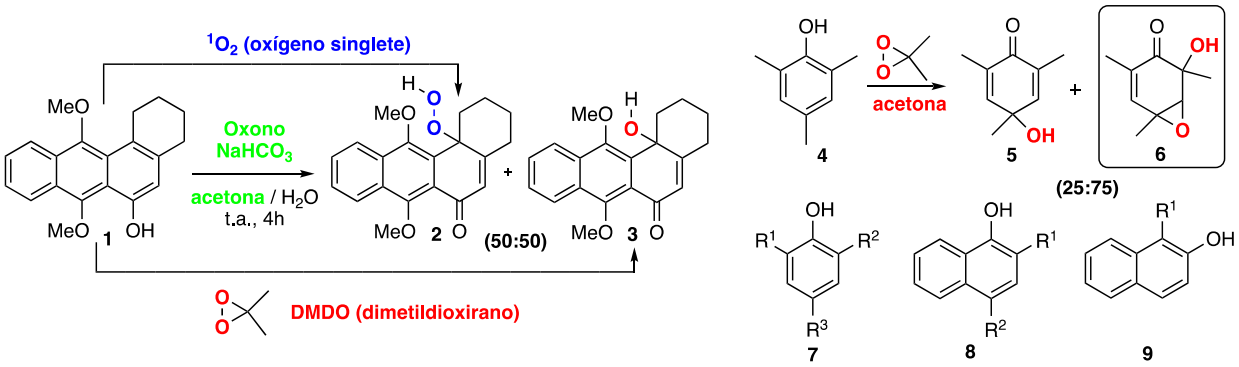
Estudio de la desaromatización oxidante de fenoles y naftoles con Oxono®/acetona como fuente de dimetildioxirano (DMDO)

E. Yonte Pindado, M. J. Cabrera, M. C. Carreño, A. Urbano*

Departamento de Química Orgánica, Universidad Autónoma de Madrid
e-mail: elena.yonte@estudiante.uam.es

***Palabras clave**: (desaromatización oxidante, fenoles, naftoles, Oxono®, dimetildioxirano)*

En nuestro grupo de investigación se ha estudiado el proceso de desaromatización oxidante de *p*-alquilfenoles, como **1**, utilizando el sistema Oxono®/$NaHCO_3$ en acetonitrilo, como fuente de oxígeno singlete, para dar *p*-peroxiquinoles, como **2**.[1] Aplicando esta metodología para la obtención de modelos tetracíclicos de anguciclinonas naturales, se observó que, al cambiar el disolvente por acetona, además del habitual *p*-peroxiquinol **2** se obtenía el *p*-quinol **3**.[2] Este hecho indicaba la presencia de un reactivo diferente al oxígeno singlete, que resultó ser el dimetildioxirano (DMDO), producido por reacción de Oxono® y acetona en medio básico.[3]



Tras diferentes ensayos de optimización, se comprobó que los fenoles 2,4,6-trisustituidos, como **4**, ofrecían los mejores resultados dando lugar mayoritariamente a desaromatización oxidante en la posición *orto* (epoxi *orto*-quinol **6**) junto con el *para*-quinol **5**, como producto minoritario. En este trabajo se pretende estudiar esta metodología sobre fenoles y naftoles diferentemente sustituidos utilizando Oxono®/$NaHCO_3$ en acetona, como fuente de dimetildioxirano. Así, se expondrán los resultados obtenidos con fenoles 2,4,6-trisustituidos (**7**) con algún grupo *t*-butilo, para comprobar el efecto estérico de este grupo voluminoso en la desaromatización oxidante selectiva de las posiciones *orto* y/o *para* con respecto al fenol. También se pretende comprobar si la metodología es aplicable a 1-naftoles (**8**) y 2-naftoles (**9**) diferentemente sustituidos.

[1] (a) Carreno, M. C.; Gonzalez-Lopez, M.; Urbano, A. *Angew. Chem. Int. Ed.* **2006**, *45*, 2737. (b) Vila-Gisbert, S.; Urbano, A.; Carmen Carreno, M. *Chem. Commun.* **2013**, *49*, 3561.
[2] Cabrera Afonso, M. J. Tesis Doctoral en curso, UAM.
[3] Adam, W.; Curci, R.; Edwards, J. *Acc. Chem. Res.* **1989**, *22*, 205-211.